The Journal of Pediatrics

VOL. 51 DECEMBER, 1957 No. 6

THE ROENTGENOGRAPHIC FINDINGS ASSOCIATED WITH NEUROBLASTOMA

CHARLOTTE F. HANSMAN, M.D. AND BERTRAM R. GIRDANY, M.D.
PITTSBURGH, PA.

THE diagnosis of neuroblastoma is based on a combination of factors. This paper reviews the chief complaints, physical findings, and laboratory data and emphasizes the roentgen findings associated with neuroblastoma in a group of 30 children seen at the Children's Hospital of Pittsburgh in the five-year period between 1951 and 1955.

REVIEW OF LITERATURE

In 1941 Wyatt and Farber[1] reviewed the roentgen changes and treatment of neuroblastoma. They concluded that there was no characteristic radiographic picture associated with the primary tumor. They discussed the type and extent of metastases. In 1937 Rypins[2] reported 3 cases of neuroblastoma with proptosis, hydrocephalus, and destructive and productive lesions in the skeleton. Abdominal masses were not palpated. Sherman and Leaming[3] in 1953 described the roentgen findings in 50 histologically proved cases of neuroblastoma. They emphasized the skeletal changes late in the course of the disease. McCrorie and Smith[4] in 1953 reported a child with neuroblastoma whose initial complaints and roentgen findings were confined to the extremities. A palpable abdominal mass and characteristic skeletal changes appeared later.

DATA

These observations are based on 30 children in each of whom the diagnosis of neuroblastoma or ganglioneuroblastoma was confirmed histologically. Sixteen patients were boys and 14 were girls. Ages ranged from 1 month to 10 years, 1 month, with 15 children in the 1 to 4 year age group. The average age was 3 years, 9 months. (Table I.)

TABLE I. AGE INCIDENCE AND SEX DISTRIBUTION

AGE GROUP (YEARS)	MALES	FEMALES
Under 1	3	3
1-4	7	8
5-9	6	2
10		1
Total	16	14

Abdominal masses were palpated in 24 instances. Fever was the chief complaint in 12 children; 9 complained of

From the Department of Radiology, Children's Hospital of Pitsburgh, and the Department of Pediatrics, University of Pittsburgh, School of Medicine.

pain in the legs, 8 were anoretic, and 7 were tired and listless. Table II lists the signs and symptoms in order of their frequency.

TABLE II. FREQUENCY OF PHYSICAL SIGNS AND SYMPTOMS IN 30 PATIENTS

Mass palpable in abdomen	24
without complaints referable thereto	5
Fever	12
Pain in legs	9
Anorexia	8
Fatigue and listlessness	7
Pain in abdomen	5
Big liver or spleen	5
Vomiting	4
Irritability and restlessness	4
Cough	3
Swelling of abdomen	3
Weight loss	2

All patients had x-ray films of the abdomen, urinary tract, and skeleton. An intra-abdominal soft tissue mass was visualized in 26 cases. In 25 the mass displaced adjacent structures (Figs. 1 and 2). Shadows of calcium density were seen in the region of an adrenal gland in 5 instances (Figs. 3 and 4), and an enlarged liver shadow was present in 5 others. Dilatation and blunting of the renal calyces indicated obstruction to drainage of the upper urinary tract by the mass in one child (Fig. 5). A large kidney shadow with attenuation of the pelvocalyceal system suggested renal infiltration in one instance. In 2 cases there was evidence of ascites and associated generalized edema of the lower extremities. Two children had mediastinal masses (Fig. 6) and 3 had extradural tumors. (Table III.)

Fourteen of the 26 abdominal masses originated in an adrenal gland. A definite site of origin could not be ascertained for any of the other 12 masses. (Table IV.)

TABLE III. ROENTGEN FINDINGS ASSOCIATED WITH THE PRIMARY TUMOR

Abdominal mass	26
Displacement of adjacent structures	25
Calcification, abdomen only	5
Enlarged liver	5
Ascites and edema	2
Hydronephrosis	1
Renal infiltration	1
Intestinal obstruction	0
Mediastinal mass	2
Obstruction on myelography	2

TABLE IV. SITE OF PRIMARY TUMOR

Abdomen	26
Adrenal gland	14
Retroperitoneal	5
Unknown	7
Mediastinum	2
Spine	3

Bony or soft tissue changes of metastatic neuroblastoma were seen in 11 children. In 3 cases the bones alone were affected and in 2 the changes were limited to the lungs and meninges. Six children had combined bony and soft tissue metastases. Pulmonary metastases were present in 4 of these cases (Fig. 7). Seven children had metastatic lesions in the skull. Four of these also had roentgen signs of increased intracranial pressure. In one instance changes in the skull were limited to signs of increased intracranial pressure. (Figs. 8 and 9.)

Eight children had lesions in the femurs and 4 showed changes in the bony pelvis (Figs. 10 and 11). In one case femoral involvement was unilateral (Fig. 12). In 3 children both tibias were affected; in 2 children only one tibia showed metastases (Figs. 13 and 14). Both humeri were affected in 2 children; in 2 others only one was involved (Fig. 15). A pathologic fracture occurred through the proximal humerus of one child (Fig. 16). There were metastases to the bones of both

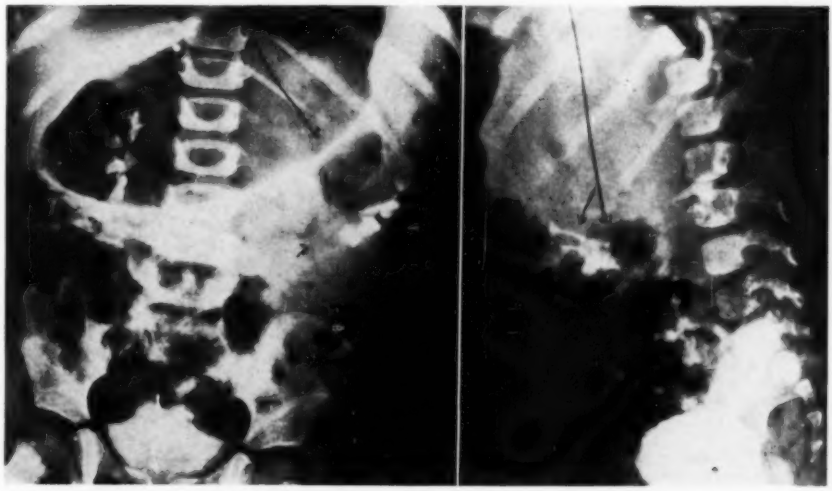


Fig. 1.—Anteroposterior and lateral films of the abdomen of a 16-month-old child show displacement of the left renal pelvis and calyces by a large suprarenal mass.

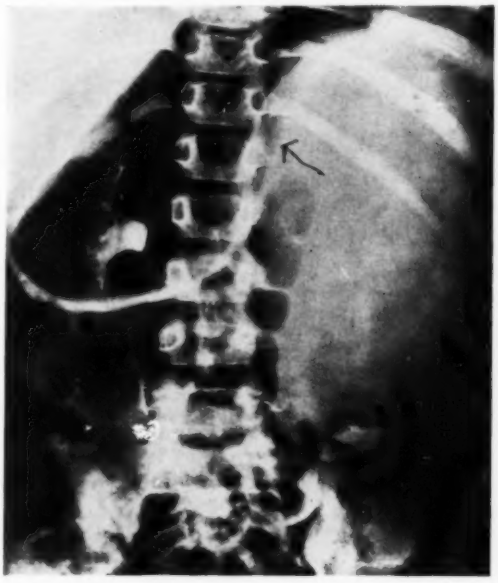


Fig. 2.—Excretory urographic film shows displacement of the air-filled stomach by a mass in the region of the left kidney in a 5-year-old child. Note the absence of visualization of renal pelvis and calyces on this side, indicating poor function of the kidney.

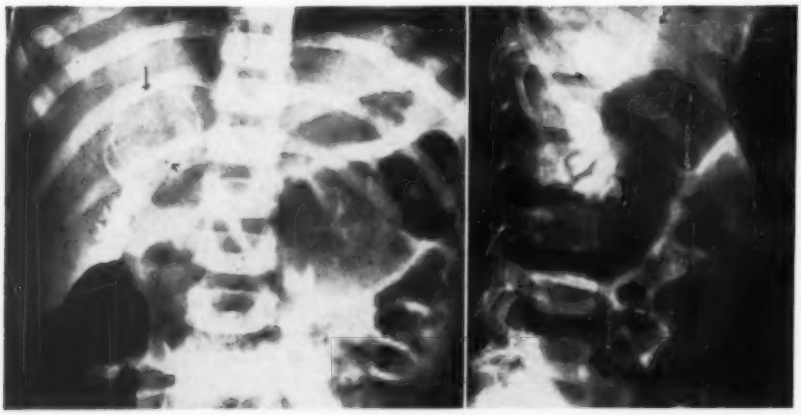


Fig. 3.—Anteroposterior and lateral excretory urographic films show a rounded shadow of calcium density in the region of the right adrenal gland in a 4½-year-old girl.

Fig. 4.—Excretory urographic film shows diffuse shadows of calcium density (arrows) in the region of the left adrenal gland in an 8-year-old girl. The left renal pelvis is displaced caudad.

Fig. 5.—Excretory urographs show marked dilatation and lateral displacement of the renal pelvis and calyces associated with a large overlying neuroblastoma.

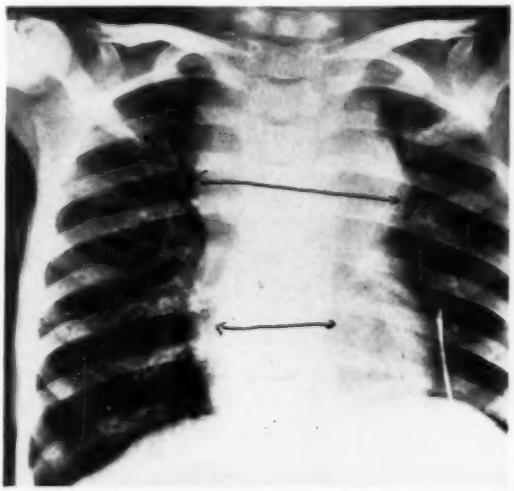


Fig. 6.—Posteroanterior film of the thorax shows a wide superior mediastinal shadow as well as paravertebral soft tissue shadows associated with involvement of the mediastinal and paravertebral structures in a 7-year-old child.

forearms in 2 instances. Three children showed evidence of skeletal metastases without skull metastases; one child with skull lesions had no demonstrable roentgen changes in the long bones. (Table V.)

TABLE V. DISTRIBUTION OF METASTASES

Lungs	4
Meninges	5
Skull	7
Femurs, bilateral	7
unilateral	1
Pelvis	4
Tibias, bilateral	3
unilateral	2
Humeri, bilateral	2
unilateral	2
Forearm, bilateral	2
Long bones without skull	3
Skull without long bones	1

teristic. The intra-abdominal soft tissue mass most commonly lies in the region of an adrenal gland, displacing adjacent structures. Urinary tract obstruction may result. The retroperitoneal tumor mass displaces the air- or barium-filled gastrointestinal tract ventrad. Intestinal obstruction is rare. Calcification within the mass suggests neuroblastoma.[3] Calcification did not occur in the mediastinal tumors.

Neuroblastoma is a malignant tumor which metastasizes the bony and nonbony structures. Small, poorly defined rounded shadows of water density in the lungs represent metastases (Fig. 7). Another roentgen indication of

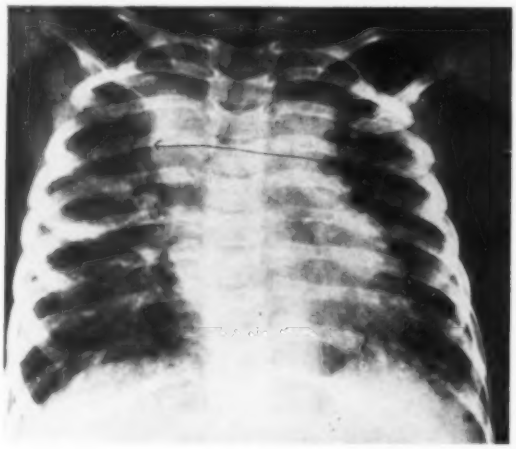


Fig. 7.—Posteroanterior film of the thorax in a 3-year-old child shows a wide superior mediastinal shadow and tiny, poorly defined nodular metastases in the lungs. Metastatic neuroblastoma was proved at necropsy.

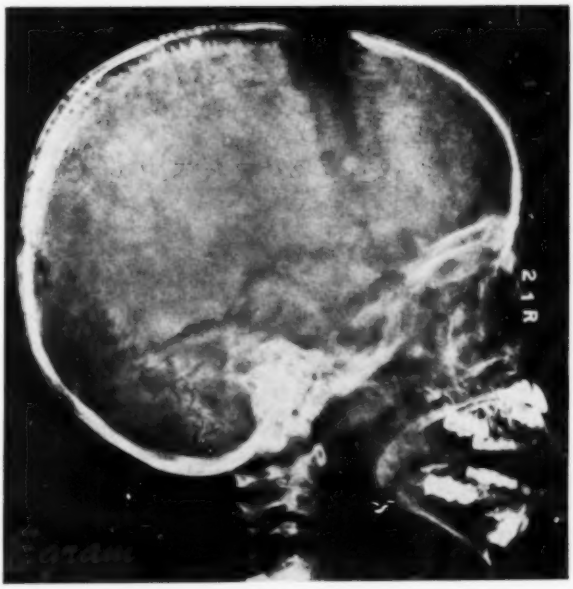
DISCUSSION

The adrenal gland is the most common primary site of neuroblastoma. The tumor may originate in any of the sympathetic ganglia. Mediastinal and spinal cord tumors are probably ganglionic in origin.

The radiographic picture associated with the primary tumor is not characsoft tissue involvement is widening of the cranial sutures due to masses of tumor tissue between the dura and the calvarium. The tumor invades the dura, which seems to act as a barrier to invasion of the brain.

A roentgenogram of the skull showing widened sutures and destruction of the bones of the cranial vault is

A.



B.

Fig. 8.—*A* and *B*, Anteroposterior and lateral films of the skull show markedly widened cranial sutures and fine mottling in the bones of the cranial vault characteristic of bone destruction. The combination of these findings is pathognomonic of neuroblastoma.

pathognomonic of metastatic neuroblastoma (Figs. 8 and 9).

The roentgen picture of metastases in neuroblastoma reflects combined destruction and proliferation of bone. The earliest evidences of metastases are tiny areas of radiolucence in either long or flat bones representing bone destruction and invasion of the marrow cavity by tumor cells. It should be emphasized that tumor cells may be detected in the bone marrow before there is roentgen evidence of their presence.

Evidence of cortical destruction is another early finding. The cortices of the medial, distal metaphyses of the femurs and the lateral aspects of the proximal tibias are frequently affected (Fig. 13). A later manifestation is subperiosteal new bone reaction as evidenced by parallel lines of calcium density along the margins of the bones. Perpendicular spiculation and extension of new bone into the surrounding soft tissue may occur (Fig. 17).

Bony metastases occurred most frequently in the skull and the femurs. The bones of the lower legs and upper extremities were late sites of involvement. In all cases of long bone involvement both metaphyses and diaphyses of the bones were affected. In no cases were the bones of the hands or feet affected.

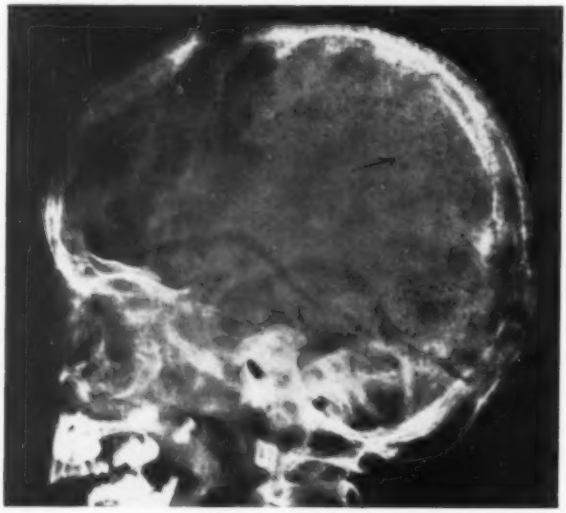


Fig. 9.—Lateral film of the skull in a 5-year-old boy terminally ill with neuroblastoma shows productive and destructive lesions (arrow) as well as markedly widened sutures.

DIFFERENTIAL DIAGNOSIS

The palpable abdominal mass is, of itself, rarely diagnostic. Neuroblastoma, Wilms's tumor, hydronephrosis, polycystic kidney, lymphosarcoma, mesenteric cyst, and renal vein thrombosis must be considered in the differential diagnosis. An occasional infant with neuroblastoma is referred with the diagnosis of enlarged spleen.

Preoperative differential diagnosis between Wilms's tumor and neuroblastoma may not be possible. Indeed,

Fig. 10.—Anteroposterior film of the femurs of a 5-year-old boy shows well the extensive productive and destructive changes in neuroblastoma. Note the subperiosteal new bone formation (arrows) as well as the diffuse mottling.

Fig. 11.—Anteroposterior film of the pelvis of the same patient shows the diffuse destructive and productive changes.

Fig. 12.—Anteroposterior film of the pelvis in an 8-year-old child shows dominantly unilateral changes on the right side. Note the subperiosteal new bone production inferior to the lesser trochanter (arrow) as well as the diffuse destructive changes.

Fig. 13.—Anteroposterior and lateral films of the knee in a 6-year-old child show well the deposition of subperiosteal new bone about the proximal portion of the shaft of the tibia. So-called "Codman's triangle" is indicated by the arrow.

Fig. 14.—Lateral film of the right knee shows a small amount of subperiosteal new bone formation about the distal portion of the shaft of the femur. This film shows well the deep soft-tissue lesion (arrows).

Fig. 15.—The humerus of a 2-year-old boy shows diffuse, tiny rounded areas of diminished density reflecting bone destruction.

Fig. 16.—Anteroposterior film of the humerus in a 6-year-old boy shows pathologic fracture through an area of bone destruction.

at surgery, accurate identification of the nature of the tumor may not be made. The final diagnosis awaits histologic proof. Wilms's tumor is an intrinsic renal mass. Nonexcretion of opaque material during excretory urography suggests Wilms's tumor. Neuroblastoma tends to displace the renal pelvis and calyces downward and laterally. In either instance neuroblastoma and Wilms's tumor may simulate one another (Fig. 2). Wilms's tumor metastasizes to the lungs and rarely to the skeleton. The major value of the excretory urogram lies in the identification of the normalcy of

the contralateral kidney. Delay films may serve to identify hydronephrosis and kindred conditions.

When the tumor has metastasized and leg or back pain brings the patient to the physician, leukemia, scurvy and malignant bone tumors must be ruled out. Tuberculosis of the spine, osteomyelitis, acute rheumatic fever, and poliomyelitis often enter the differential diagnosis. The skeletal changes of leukemia and metastatic neuroblastoma are radiographically indistinguishable. Involvement of the skull is less common in leukemia.

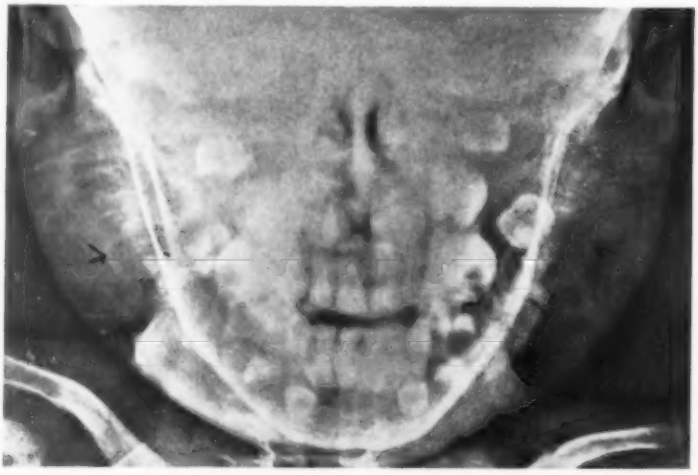


Fig. 17.—Anteroposterior film of the mandible in a 5-year-old boy shows perpendicular spiculation associated with deposition of new bone at the sites of metastasis.

Bone marrow aspiration is useful in establishing a diagnosis which otherwise depends upon the microscopic examination of tissue obtained at surgery. Roentgen changes in the long bones may dictate an optimal site of bone marrow study. Marrow study may reveal tumor cells in the presence of radiographically normal bone. Four of the 11 children having bone marrow smears which were positive for tumor cells did not show abnormal roentgenographic changes in their bones.

SUMMARY AND CONCLUSIONS

1. The roentgen findings, chief complaints, and physical signs associated with 30 microscopically proved cases of neuroblastoma are presented.

2. An intra-abdominal mass is the most frequent finding on both physical and x-ray examination. The mass is a nonspecific finding and involves the differential diagnosis of all intra-abdominal masses.

3. Roentgenograms of the skull showing widened sutures and evidence of destruction of the bones of the cranial vault are pathognomonic of metastatic neuroblastoma.

4. The differential diagnosis of neuroblastoma is presented.

The radiographic illustrations in this paper are LogEgrams produced from the Log-Etronic printer. The authors are indebted

to Dr. Elmer G. St. John of Binghamton, New York, and to LogEtronics Inc., for making these reproductions.

REFERENCES

1. Wyatt, Geo. M., and Farber, Sidney: Neuroblastoma Sympatheticum Roentgenological Appearances and Radiation Treatment, Am. J. Roentgenol. **46**: 485, 1941.
2. Rypins, E. L.: The Roentgen Diagnosis of Neuroblastoma in Children, Am. J. Roentgenol. **37**: 325, 1937.
3. Sherman, Robert S., and Leaming, Robert: The Roentgen Findings in Neuroblastoma, Radiology **60**: 837, 1953.
4. McCrorie, W. D. C., and Smith, A.: Sympathicoblastoma (Adrenal Neuroblastoma) With Report of a Case, Brit. J. Radiol. **26**: 207, 1953.

Enlargement of the Breast in the Newly Born Infant

It occasionally happens, that children newly born are found to have their breasts swollen, and evidently inflamed. This exists in various degrees, from a slight tumefaction, to one that threatens suppuration.

There is a vulgar opinion, that these enlargements proceed from a quantity of milk within these little bodies, which must be squeezed or milked out, that mischief may not follow. This absurd opinion, has, unfortunately, led to the preposterous, and mischievous practice just alluded to; in consequence of which, the parts have become so irritated, as to occasion much pain, and increase of inflammation. The little tumour has been violently pressed, with the view to force out impacted milk; but being disappointed in its not appearing, the pressure is renewed again, and again, and each effort with an increase of force; since, agreeably to them, if the cause be not removed, serious consequences will follow to the parts, and, perhaps, in females for ever, destroy their usefulness. In thus pursuing a bad theory, by a worse practice, the consequences which they so much dreaded, have absolutely taken place: suppuration has sometimes followed these rude manoeuvres, and has for ever destroyed the organization of these most useful parts.

It cannot, therefore, be too peremptorily forbidden, that these parts should be meddled with; for all that is necessary to their restoration, is a little time; or the application of a piece of linen, moistened with a little sweet oil, unless the tumours be unusually large, and the inflammation very considerable. In this case, a bread and milk poultice, renewed every three or four hours, will be almost sure to restore them to health in a few days.

WILLIAM DEWEES, ON CHILDREN, 1834.

URINARY EXCRETION OF FLUORIDE BY CHILDREN AGED TWO THROUGH FIVE YEARS USING A STANNOUS FLUORIDE-CONTAINING DENTIFRICE IN A NATURAL FLUORIDE AREA AND A NONFLUORIDE AREA

RICHARD A. SCHWEINSBERGER, M.S., AND JOSEPH C. MUHLER, D.D.S., PH.D.
BLOOMINGTON, IND.

RECENTLY, fluoride-containing dentifrices have been introduced into the commercial market for the partial reduction of dental caries in children. The clinical evidence available to evaluate the effectiveness of those dentifrices containing sodium fluoride indicates that they have no significant effect as anticariogenic agents,[1] but the use of a stannous fluoride-containing dentifrice has been shown by Muhler and others[1-3] and recently corroborated by Jordan and Peterson[4] to have a significant anticariogenic effect. However, the use of any fluoride-containing dentifrice by young children whose teeth are in the process of calcification has raised the question of the possibility that such a dentifrice may increase the blood fluoride level to such a degree that an increased incidence of mottled enamel may result. To learn more about this problem a urinary fluoride study was conducted with male children, all of whom were under 6 years of age, who used a commercially available stannous fluoride dentifrice, and who lived in two different fluoride areas: (1) an area having a naturally fluorinated communal water supply (F — 1.10 μg per milliliter); and (2) an area with a low concentration of fluorine in the communal water supply (F — 0.10 μg per milliliter). The urinary fluoride level is a dependable index of the fluoride ingested, since urinary fluoride output closely parallels any increase in fluorine intake.[5]

It has been shown previously that the use of a stannous fluoride dentifrice does not increase the urinary fluoride output of school-age children[6] whether they lived in a naturally fluoridated area (F — 0.80 μg per milliliter) or a fluoride-low area (F — 0.10 μg per milliliter). It is generally accepted that children consuming water containing 1.0 ppm fluorine from birth benefit by a reduction in the incidence of dental caries[7] and do not demonstrate any degree of endemic cumulative toxic fluorosis or toxicity as judged by a long-term pediatric survey of children residing in such an area.[8]

EXPERIMENTAL PROCEDURE

This study was divided into two series. Series I was composed of male children who were permanent residents of a natural fluoride area, Greenfield, Indiana, where the communal water supply is naturally fluorinated at a

From the Department of Chemistry, Indiana University.

This study was supported in part by a grant from The Procter and Gamble Company, Cincinnati, Ohio.

concentration of 1.10 ppm. Series II consisted of male children who lived in a nonfluoride area, Bloomington, Indiana, where the communal water supply contains 0.10 ppm fluoride. All of the children in series II resided in one university housing development.

The children in series I were divided into two groups with ages ranging from 2 through 5 years. There were 60 children in this series divided equally between the control (group 1) and the experimental (group 2) group. Series II consisted of 90 children of the same age range as used in series I and was divided into a control (group 1) and the experimental (group 2) group. The children in series I were divided at random into either group 1 or 2, while the children in series II were divided according to their urinary fluoride level in order to obtain a better balance between the two groups. Both series I and series II followed an identical pattern of investigation.

Both series were studied during three periods—a precontrol, experimental, and a postcontrol period. During the precontrol period both the control and the experimental groups used a nonfluoride dentifrice. This period lasted for 6 weeks in series I and 5 weeks for series II. At the termination of the precontrol period, one-half of the children remained on the control nonfluoride dentifrice and the other one-half were placed on the experimental stannous fluoride dentifrice.* This experimental period lasted for 10 weeks for both series. The last part of each study consisted of a postcontrol period, in which both groups again used the nonfluoride-containing dentifrice. This period lasted for 3 weeks in series I and 5 weeks in series II.

In both series urine was collected from all the children biweekly and chemically analyzed for fluoride by methods previously described.[4] All of the urine was collected for a 24-hour sample period, in as far as this was possible for young children. An exacting 24-hour specimen was not attempted in order to be able to determine the total daily fluoride output because of the variable bladder training of the young children and because much previous work, in which a total 24-hour specimen was collected, has indicated that a biweekly analysis of urine collected through the entire day produces almost exactly the same relative data as that obtained on the basis of an entire 24-hour specimen.[5, 6]

DATA AND DISCUSSION

The data from this experiment are seen in Tables I and II. Table I shows the urinary fluoride excretion for the children in the control and experimental groups in the naturally fluorinated area (series I). A total of 45 of the 60 children finished the study with 24 in the control group and 21 in the experimental group having samples available throughout the entire study period. The mean age of the control group was 3.89 years and that of the experimental group was 4.64 years. The urinary fluoride data are presented according to the precontrol, experimental, and the postcontrol periods for both the control and experimental groups. Also, the urinary data within each of the three periods are shown according to their weekly excretion values. At

*The composition of the dentifrice used in this study was as follows: heat-treated orthophosphate, 42 per cent; detergent (nonsoap), 2 per cent; humectant, 25 per cent; water, 29.2 per cent; binder, 1.4 per cent; stannous fluoride, 0.4 per cent; and flavor.

TABLE I. COMPARISON OF MEAN VALUES OF URINARY FLUORIDE EXCRETION FOR ALL SUBJECTS 2 TO 5 YEARS OF AGE TABULATED BY WEEKS FOR THE CONTROL GROUP AND THE EXPERIMENTAL GROUP FOR EACH PERIOD IN THE TEST

(Natural Fluoride Area, Greenfield, Indiana; F = 1.10 ppm in Communal Water Supply)

	GROUP 1, CONTROL (MEAN AGE: 3 YR., 11 MO.)			GROUP 2, EXPERIMENTAL (MEAN AGE: 4 YR., 8 MO.)	
	WEEK NO.	NO. OF SUBJECTS	URINARY F (μG/ML.)	NO. OF SUBJECTS	URINARY F (μG/ML.)
Precontrol period (both groups on a nonfluoride dentifrice)	1	9	0.66	20	0.83
	2	10	0.91	20	0.91
	3	21	0.69	21	0.95
	4	22	0.67	20	0.92
	5	19	0.72	17	0.83
	6	25	0.76	20	0.95
	Mean (all samples)		0.72		0.91
Experimental period (control group on nonfluoride dentifrice and the experimental group on the stannous fluoride-containing dentifrice)	1	22	0.70	16	1.00
	2	20	0.77	20	0.89
	3	23	0.61	21	0.91
	4	21	0.64	21	0.82
	5	21	0.62	20	0.91
	6	22	0.63	21	0.83
	7	24	0.64	21	0.81
	8	23	0.52	21	0.73
	9	21	0.59	21	0.66
	10	23	0.58	19	0.81
	Mean (all samples)		0.63		0.82
Postcontrol period (both groups using a nonfluoride dentifrice)	1	22	0.54	20	0.81
	2	22	0.72	20	0.78
	3	19	0.69	19	0.81
	Mean (all samples)		0.66		0.80

the termination of the first six-week period (the precontrol period), when both groups were using the nonfluoride dentifrice, there was a mean urinary fluoride concentration of 0.72 and 0.91 μg per milliliter for the control and experimental groups, respectively. During the following 10 weeks the control groups remained on the nonfluoride dentifrice and the experimental group received the stannous fluoride dentifrice. At the end of this period the mean urinary fluoride value for the control group was 0.63 μg per milliliter and the experimental was 0.82. This represents an approximate decrease of 12 per cent in the former group and 10 per cent in the latter group. These data clearly demonstrate that the use of the stannous fluoride-containing dentifrice was not associated with any increased urinary fluoride output even though the children resided in a naturally fluoridated area. The mean urinary fluoride excretion at the end of the posteontrol period suggests similar conclusions.

Table II shows the urinary fluoride excretion for the children in series II who used the control and fluoride dentifrice in the nonfluoride area. A total of 76 of the 90 children finished the study, with 38 subjects each in the control and the experimental groups having samples available throughout the entire study period. The mean age of the control group was 3.17 years and of the experimental group 3.24 years. The data indicate similar conclusions as those reported for series I,

TABLE II. COMPARISON OF MEAN VALUES OF URINARY FLUORIDE EXCRETION FOR ALL SUBJECTS 2 TO 5 YEARS OF AGE TABULATED BY WEEKS FOR THE CONTROL GROUP AND EXPERIMENTAL GROUP FOR EACH PERIOD OF THE TEST

(Low Fluoride Area, Bloomington, Indiana; F = 0.10 ppm in Communal Water Supply)

	GROUP 1, CONTROL (MEAN AGE: 3.17 YR.)			GROUP 2, EXPERIMENTAL (MEAN AGE: 3.24 YR.)	
	WEEK NO.	NO. OF SUBJECTS	URINARY F (μG/ML.)	NO. OF SUBJECTS	URINARY F (μG/ML.)
Precontrol period (both groups on a nonfluoride dentifrice)	1	10	0.32	5	0.35
	2	24	0.31	22	0.35
	3	29	0.31	28	0.30
	4	38	0.30	38	0.30
	5	38	0.30	38	0.32
	Mean (all samples)		0.30		0.31
Experimental period (control group on a nonfluoride dentifrice and the experimental group on the stannous fluoride-containing dentifrice)	1	38	0.29	38	0.32
	2	38	0.29	38	0.31
	3	38	0.30	38	0.35
	4	38	0.30	38	0.32
	5	38	0.27	38	0.29
	6	38	0.28	38	0.27
	7	38	0.27	38	0.28
	8	38	0.29	38	0.30
	9	38	0.29	38	0.31
	10	38	0.30	38	0.31
	Mean (all samples)		0.29		0.30
Postcontrol period (both groups using a nonfluoride dentifrice)	1	9	0.31	13	0.28
	2	28	0.28	27	0.31
	3	37	0.32	38	0.34
	4	38	0.32	38	0.32
	5	27	0.33	28	0.37
	Mean (all samples)		0.32		0.33

i.e., that the use of a stannous fluoride-containing dentifrice does not increase the urinary fluoride excretion level. The mean urinary fluoride values for the children in series II are considerably less than those in series I. This is as would be expected since there is approximately a tenfold increase in the fluoride concentration of the water which is received by the children in series I. However, taking both series collectively, these data would strongly suggest that the routine use of a stannous fluoride dentifrice is not associated with any perceptible increase in the urinary fluoride level in children 2 through 5 years old regardless of whether they receive an optimal fluoride drinking water (F = 1.10 μg per milliliter) or a fluoride-deficient communal water supply.

CONCLUSIONS

The data of this investigation indicate that the routine use of a stannous fluoride-containing dentifrice (F = 1,000 μg per gram) was not associated with any increased retention of fluorine in the body as indicated by the urinary fluoride level of those young children in the age range of 2 through 5 years, regardless of whether they use either a natural fluoride communal water supply or a nonfluoride-containing communal water supply.

REFERENCES

1. Muhler, J. C., Radike, A. W., Nebergall, W. H., and Day, H. G.: A Comparison Between the Anticariogenic Effects of Dentifrices Containing Stannous Fluoride and Sodium Fluoride, J. A. D. A. 51: 556, 1955.
2. Muhler, J. C., Radike, A. W., Nebergall, W. H., and Day, H. G.: The Effect of a

Stannous Fluoride-containing Dentifrice on Caries Reduction in Children, J. Dent. Res. 33: 609, 1954.
3. Muhler, J. C., Radike, A. W., Nebergall, W. H., and Day, H. G.: The Effect of a Stannous Fluoride-containing Dentifrice on Dental Caries Reduction in Children. II. Caries Experience After One Year, J. A. D. A. 50: 163, 1955.
4. Jordan, W. A., and Peterson, J. K.: Caries-inhibiting Value of a Dentifrice Containing Stannous Fluoride: First Year Report of a Supervised Toothbrushing Study, J. A. D. A. 54: 589, 1957.
5. McClure, F. J.: Nondental Physiological Effects of Trace Quantities of Fluorine, in Dental Caries and Fluoride, F. R. Moulton, Editor, American Association for the Advancement of Science, 1946, p. 77.
6. Schweinsberger, R. A., and Muhler, J. C.: Urinary Fluorine Levels in Children Following the Clinical Use of a Stannous Fluoride-containing Dentifrice, J. Dent. Res. 35: 760, 1956.
7. Hatton, W. L., Linscott, B. W., and Williams, D. B.: Brantford, Ontario, Fluoridation Study, J. A. D. A. 49: 183, 1954.
8. Schlesinger, E. R., Overton, D. E., and Chase, H. C.: A Long-Term Medical Study of Children in a Community With a Fluoridated Water Supply, in Fluoridation as a Public Health Measure, J. H. Shaw, Editor, American Association for the Advancement of Science, 1954, pp. 131-147.

INTERSTITIAL PLASMA CELL PNEUMONIA AND PNEUMOCYSTIS CARINII

ANÍBAL ARIZTÍA, M.D., WERNER BUSTAMANTE, M.D., LUIS MORENO, M.D., ARMANDO DOBERTI, M.D., CLARA ROMÁN, TULIO PIZZI, M.D., AND MARÍA DÍAZ, M.D., SANTIAGO, CHILE

IN THE last few years, an increasing number of papers from European clinics have been published describing a severe respiratory disease which almost exclusively attacks premature and undernourished infants. The pathological findings show widespread interstitial infiltration of the lungs with mononuclear cells and plasmocytes and a peculiar foamy exudate in the alveola. Most cases appear in an epidemic manner, in wards of children's hospitals. The etiology has not been definitely established, although several years ago, Vanek and Jirovec[1] called the attention to the presence in these cases of a parasite Pneumocystis carinii, known to infect a wide variety of animals. These findings have been confirmed by a number of authors, but controversy still exists in regard to the exact role played by this parasite and to the possibility of other etiological factors being involved.[12-14]

In 1953 Deamer and Zollinger[2] published a review of this disease and stated that it seemed to be relatively unknown in America. Nelson[3] in his textbook says that it has not been reported in the United States and that the disease is probably limited to central and northern European countries. In 1955, Lunseth[4] published one case, considered to be the first in the United States. Sternberg and Rosenthal,[5] in 1955, presented four cases seen in a U.S. Army Hospital in Bad Cannatatt, Germany, which occurred in infants from German orphan homes. They stressed the fact that both doctors and nurses agreed that this was a different type of respiratory illness that they had not seen before.

In South America no reports were published of the disease until 1954, although the parasite was first seen in Brazil by Chagas[6] in 1909 in laboratory animals. In 1954, Donoso and Meyerstein[7] reported on six cases of interstitial pneumonia that appeared in epidemic character on the infant ward of the maternity division of the Hospital El Salvador in Santiago, Chile. The pathological findings in some of those cases were similar to those described by the European pediatricians. No etiological agent was found, but no parasitological investigation was made because the authors suspected a virus origin.

Since 1951, Professor Ariztía, of our hospital, has believed that the disease was to be found in Chile, and the clinical diagnosis was made in several instances. In 1953, several cases of interstitial pneumonia were reported by

From the Department of Pediatrics and the Department of Parasitology, School of Medicine, University of Chile.

Address: Children's Hospital "Calvo Mackenna," 248 Antonio Varas, Santiago, Chile.

Zelada and colleagues,[8] from our hospital. Since 1953, our pathologist, Dr. Moreno, has been interested in the histological findings in some special types of respiratory diseases diagnosed during life as bronchopneumonia and occurring in premature and undernourished infants. Studying these cases, we noticed that they were in all aspects similar to those described by the European pediatricians as interstitial plasma cell pneumonia. Further, with the collaboration of the Department of Parasitology of the University of Chile, the presence of the parasite *Pneumocystis carinii* in lung sections from these patients was demonstrated.[15]

In this paper, the first ten cases in Chile of interstitial plasma cell pneumonia in which *Pneumocystis carinii* was present are reviewed.

MATERIAL

All our cases are from the Children's Hospital "Luis Calvo Mackenna" Santiago, Chile. A clinical diagnosis of interstitial plasma cell pneumonia was made in five cases; in the others, the clinical diagnosis was bronchopneumonia.

Clinical Description.—Family history was not contributory. Seven of the cases occurred in premature and two in full-term infants. In one case, the birth weight was unknown. The onset of the disease occurred between 3 and 6 months after birth (Figs. 1 and 2). With reference to the nutritional condition we found that all of the infants were undernourished. Seven of our patients had been admitted to the infant ward more than two months

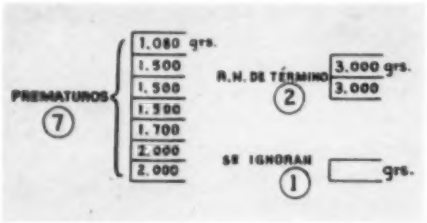


Fig. 1.—Birth weight and prematurity in cases observed.

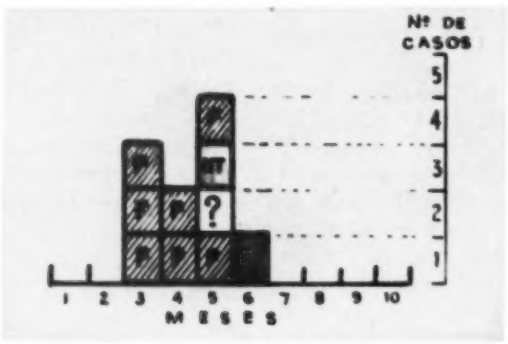


Fig. 2.—Age at onset of disease.

previous to the onset of the disease; two were discharged from the same ward and readmitted a few days later with a clinical picture diagnosed as bronchopneumonia.

The clinical onset is difficult to determine because early signs and symptoms are often mild, not specific, and frequently even lacking. However, in six cases the onset was characterized by increasing dyspnea, cyanosis, and loss of appetite. In four cases there was a sudden onset. Fever was moderate and never higher than 38° C. Only in one case was a persistent high fever observed. The weight curve was stationary only in four cases.

Physical Examination.—The respiratory distress was very marked, and there was an anxious expression on the face. Percussion of the lungs was negative, except in one case where hyperresonance as a consequence of a pneumothorax was noted. Auscultation was negative in four cases. In six, moderate crepitations and râles were noted. This striking discrepancy between dyspnea and the lack of physical symptoms is very important for clinical guidance in establishing the diagnosis.

Clinical Types.—The clinical course was variable and in accordance with Torricelli's criteria[9]; seven were typical cases of interstitial plasma cell pneumonia. In two cases the clinical type was similar to bronchopneumonia. One case was of the asphyxia type with pneumothorax.

The duration of the disease in two cases was less than one week; in three, about two weeks; and in five, more than two weeks.

Laboratory Examination.—The Kahn reaction was negative in all cases. The blood count was not characteristic, and the urinalysis was normal. Tuberculin tests were negative. Cold agglutinins were not performed.

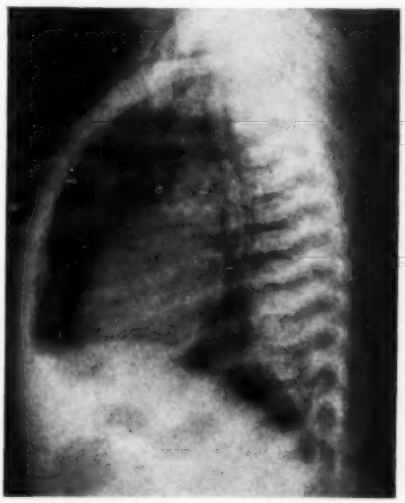


Fig. 3.—Radiological aspect in lateral view showing marked emphysema.

X-ray Study.—The radiological findings are so characteristic that, although they do not present a unique pattern, the constant association of the different findings makes the radiological picture almost pathognomonic. The experienced radiologist may be able to make the diagnosis even by simple fluoroscopy. There is an extremely severe persistent interstitial emphysema that flattens and immobilizes the diaphragm, causing at the same time a protrusion of the aerated lung parenchyma through the intercostal spaces. There is also a mediastinal emphysema, especially visible in lateral position. The parenchymal findings vary from normal aspect to a micronodular infiltration in the posterior portions of both

Fig. 4.

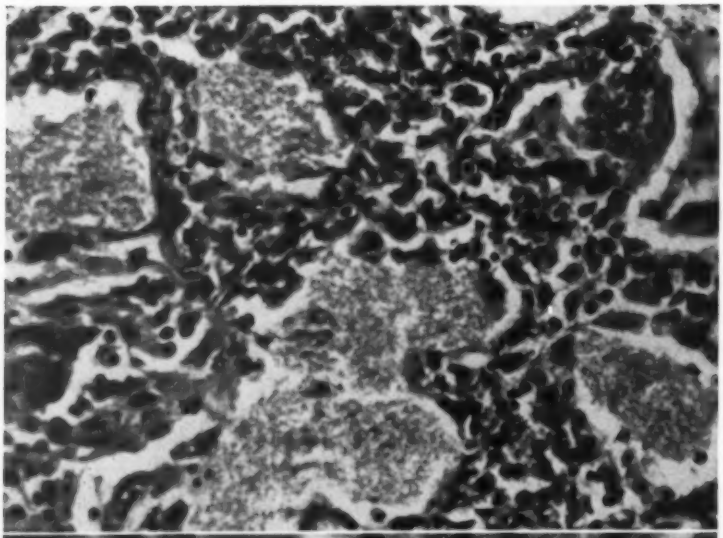


Fig. 5.

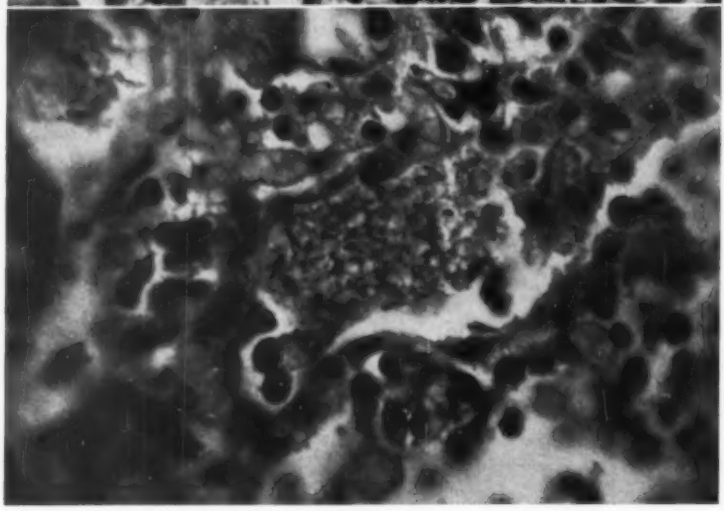


Fig. 4.—Section of a lung stained by Maximow technique. (×400.) Notice the interstitial infiltration and the foamy exudate in the alveola.

Fig. 5.—Section of a lung stained by Maximow technique. (×800.) Notice detail of foamy exudate in the alveola. Some parasites can be observed.

lungs, which is the most common picture observed. Peribronchial infiltrations, lobar or segmentary, are also seen. Most constant is an emphysema which is not related to the clinical picture, which is found previous to the development of symptoms and persists after they have disappeared (Fig. 3).

Treatment.—We used various antibioties (penicillin, Chloromycetin, Aureomycin, Terramycin, Achromycin) without result. Initially we used penicillin with streptomycin, and as soon as we suspected interstitial plasma cell pneumonia, a change was made to a broad-spectrum antibiotic. In six cases the antibioties were combined with cortisone. All our patients were placed in an oxygen tent and given special routine care.

Anatomical Findings.—Macroscopic study: The lungs were enlarged, and on their surface some costal markings and emphysematous bullae were found. Their color was dark red, with a lighter tinge toward the anterior borders. The consistency was increased, with a tendency to rigidity toward the posterior surface. On section, the surface appeared dark red, smooth, solid, with air only in the anterior borders.

Microscopic study: Histologically there was thickening and infiltration of plasmatic cells in the interalveolar and peribronchial septa.

In the alveoli, isolated histiocytic elements, sometimes forming syncytial masses, and a foamy exudate (beehive pattern) that contained small chromatic formations were found (Figs. 4 and 5).

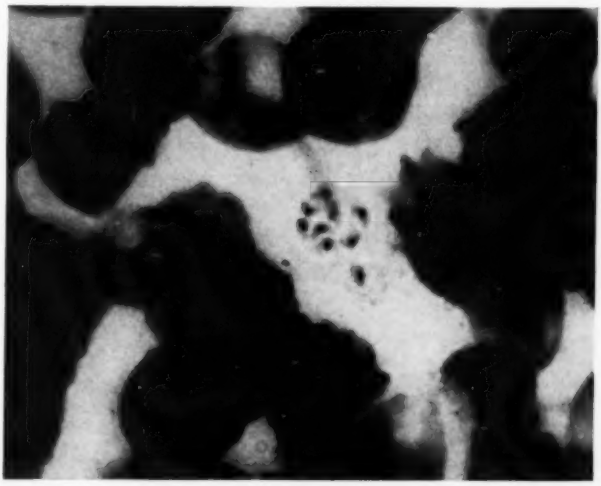


Fig. 6.—Lung smear stained with May-Grünwald-Giemsa. (×1,200.) Notice a typical "rosette-like" structure of *Pneumocystis carinii*.

The histological samples should be taken from the deeper and darker lung zones. Both van Gieson and hematoxylin-eosin stains are enough for diagnostic purposes, but for the better identification of the plasmatic cells other techniques should be used.

Frequently, the interstitial plasma cell pneumonia was associated with

bronchopneumonia as well as atelectasis with hyaline membranes.

Parasitological Study.—The parasites may be found in histological sections and in lung smears. In the latter the identification is easier because the typical "rosette-like" formation is clearly seen. In sections the parasites appear mainly in the foamy exudate which fills the alveolus. They are tiny elements, with an average diameter of 1 to 3 microns and are easily distorted by fixation. Nevertheless, with some staining methods (Maximow and silver techniques) they are easily identified. Some of them consist of a portion of cytoplasm of round or oval shape with a deeply stained central nucleus; other are more or less elongated, resembling Toxoplasma, although smaller. It is also possible to find elements with several nucleus and typical "rosette-like" structures composed of eight independent parasites included in a common membrane (Fig. 6).

DISCUSSION

There is a little doubt but that many cases of a peculiar respiratory disease, described in recent years in the European literature, can be considered as a pathological entity. This has been named interstitial plasma cell pneumonia. The more striking factors are the scarcity of physical signs, associated with severe functional and systematic involvement; the high mortality rate; the typical pathological findings which show an interstitial infiltration of round cells and plasmocytes, and foamy alveolar exudate in which a sporozoan-like parasite can be found; and, finally, the epidemic character affecting almost exclusively premature and/or undernourished infants. All these characters were clearly present in our cases.

In differential diagnosis one must consider the different types of viral pneumonitis (Adams[10]) bacterial bronchopneumonia, spastic bronchitis, and foreign bodies in the air tract.

A complement deviation test, which uses as antigen extracts of lungs of infants that have died of interstitial plasma cell pneumonia constitute a new aid in the diagnosis of this disease. We did not use this test in the reported cases, but at present we perform it in all suspected cases and their contacts.

The main problem is the possible etiological factors. The constant finding of a parasite, *Pneumocystis carinii,* in the exudate and the absence of any other evident etiology strongly point to the possibility that this parasite may be causal agent. Nevertheless, definite proof is still lacking, as it has not been possible to cultivate the parasite in artificial media. The experimental inoculations in animals have generally failed, although some recent workers have reported successful results.

The taxonomy of *Pneumocystis carinii* is debatable. Most authors consider it a protozoan; others consider it a fungus, although their views are erroneous according to Westphal.[11] The possibility that a virus could be associated, the parasite being only a secondary invader, must be considered. On the other hand, direct attempts to isolate a virus have so far been unsuccessful, and the pathological features are quite different from those currently observed in virus pneumonitis. In any case, the exact nature of *Pneumocystis carinii* and its relationship with inter-

stitial plasma cell pneumonia are challenging problems which require research.

One thing seems clear. The disease attacks only infants with poor nutrition. An adequate consideration of these factors ought to be of paramount importance in the prevention and treatment of this disease.

SUMMARY

Interstitial plasma cell pneumonia in infants with demonstration of *Pneumocystis carinii* in lung tissue was found in ten cases in Santiago, Chile. These cases are the first reported in South America.

A clinical radiological and parasitological study of these cases is presented with a short review of the literature on the subject.

The etiological role of *Pneumocystis carinii* as the causative agent of the I. P. C. P. is discussed.

REFERENCES

1. Vanek, J., and Jirovec, O.: "Parasitare Pneumonien" interstitelle Plasmazellenpneumonie der Frühgeborenen, verursacht durch Pneumocystis carinii, Zentralbl. Bakt. I Abt. Orig. **158**: 120, 1952. (Reference in Trop. Dis. Bull. **49**: 908, 1952.)
2. Deamer, W. C., and Zollinger, H. U.: Interstitial "plasma cell" pneumonia of Premature and Young Infants, Pediatrics **12**: 11, 1953.
3. Nelson, W.: Textbook of Pediatrics, ed. 6, Philadelphia, 1954, W. B. Saunders Co.
4. Lunseth, J., Kirmse, T., Prezyna, A., and Gerth, R.: Interstitial Plasma Cell Pneumonia, J. PEDIAT. **46**: 137, 1955.
5. Sternberg, S., and Rosenthal, J.: Interstitial Plasma Cell Pneumonia, J. PEDIAT. **46**: 380, 1955.
6. Chagas, C.: Nova tripanozomiase humana, Mem. Inst. Oswaldo. Cruz. **1**: 159, 1909.
7. Donoso, S., and Meyerstein, O.: Consideración anátomo pathológica sobre seis casos de neumonía interstitial, Arch. Hosp. R. del Río **21**: 29, 1954.
8. Zelada, H., Winter, A., Vargas, A., Matte, R., and Ibañez, S.: Neumonía intersticial, Rev. Chilena de Ped. **24**: 340, 1953.
9. Torricelli, C.: Attualitá sulla polmonite interstiziale plasma-cellulare, Il Lattante **26**: 214, 1955.
10. Adams, J. M.: Primary Virus Pneumonitis With Cytoplasmatic Inclusion Bodies, J. A. M. A. **116**: 925, 1941.
11. Westphal, A.: Zur Diagnose der Pneumocystis carinii-Infektion des Menschen, Ztschr. Tropenmed. u. Parasitol. **4**: 549, 1953.
12. Jirovec, O.: Ueber die durch Pneumocystis carinii Verursachte interstitiellen Pneumonie der Saulinge, Monatsschr. Kinderh. **102**: 476, 1954.
13. Jirovec, O.: Nové pozomatky o pneumocystose kojenku". Ceskolov. Hyg. Epidemiol., Mikobiol. Immunol. **4**: 389, 1955. (Reference in Trop. Dis. Bull. **53**: 668, 1956.)
14. Le Tan Vinh: La pneumonie a pneumocystis. Ses rapports avec la pneumonie interstitelle a plasmocytes, Arch. franc. Pediat. **11**: 1035, 1954.
15. Pizzi, T.: Comprobación de pneumocystis carinii en casos de neumonía intersticial plasmocitaria, Bol. Chil. Paras. **11**: 16, 1956.

COMPARISON OF OCULAR REACTIONS USING PENICILLIN AND BACITRACIN OINTMENTS IN OPHTHALMIA NEONATORUM PROPHYLAXIS

A. M. Margileth, Commander (MC) USN
Chelsea, Mass.

SEVERAL years ago we became concerned about the high incidence of severe ocular reactions in the newborn infant's eyes following the use of silver nitrate. In view of these frequent reactions to silver nitrate which have been reported as high as 100 per cent,[1, 2] three years ago we began using penicillin ophthalmic ointment. It was immediately apparent that fewer reactions occurred. Two and one-half years ago we undertook a controlled study* to determine the frequency and severity of ocular reactions using penicillin and bacitracin ophthalmic ointments. The disadvantages of using penicillin in ophthalmia neonatorum prophylaxis were reviewed during a recent round table conference[3] of ophthalmologists who pointed out that penicillin was ineffective against most gram-negative organisms. Most physicians are well aware of the severe ocular reaction that may occur after a few instillations of penicillin ophthalmic ointment. It also may be possible to sensitize the infant to penicillin at birth so that a systemic reaction might occur later in life when penicillin is given again. Bacitracin is bactericidal and is effective against many coccal (including the gonococcus) and some bacillary forms. It is virtually nontoxic when used topically, and its potency is stable. It would rarely be used systemically later in life compared to penicillin. Primary hypersensitivity reactions to bacitracin are rare, and allergic manifestations are practically nil.[4, 5]

Several authors[6, 7] have advocated that no prophylaxis be given at all or that simple irrigation of the eyes with saline[7] or washing with Zephiran solution[8] be done. These suggestions are the result of a decreased frequency of gonorrhea ophthalmic infections in the newborn period, and the ability of antibiotics to control such infections quickly when they occur. This was pointed out by Schultz and Hartmann in Germany,[9] Waehter and Pennoyer[10] in this country, and more recently in a resolution adopted by the Health Department of the City of New York.[11] The Board of Health of the City of New York repealed a section of the sanitary code which removed the requirement that prophylactic measures of any sort had to be taken at the birth of a child for the prevention of ophthalmia neonatorum. Schultz and Hartmann[9] and Lehrfeld[12] also noted

From the U. S. Naval Hospital, Corona, Calif.

The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

Present address: U. S. Naval Hospital, Chelsea, Mass.

*Through the courtesy of Malcolm H. Merrill, M.D., Director of Public Health, State of California, Berkeley.

the high incidence of untoward reactions with silver nitrate and reported eighteen cases of gonorrhea ophthalmia neonatorum which occurred after silver nitrate prophylaxis had been given. The purpose of this study was to evaluate the type of ocular reaction to bacitracin and penicillin ophthalmic ointments and to determine if possible their effectiveness in preventing infections of the newborn infant's eyes.

MATERIALS AND METHODS

This study was carried out in the newborn section of the Pediatric Service of the U. S. Naval Hospital, Corona, California. From Jan. 1, 1953, until Aug. 27, 1954, silver nitrate (1 per cent in wax ampules) was used in 2,250 infants. The eyes were irrigated with saline immediately following the instillation of 1 or 2 drops of the silver nitrate solution. The physical limitations of a small nursery and a small post-partum bed capacity necessitated using the rooming-in plan so that most of the infants were taken to their mothers by 24 to 36 hours of age. Frequent complaints were made by the mothers about the red swollen eyelids and the purulent discharge which occurred often during the first few days. Although an accurate account was not maintained, well over 50 per cent of the newborn infant's eyes showed a mild to severe chemical conjunctivitis during the first three to four days which was the usual duration of hospitalization.

The comparative study using penicillin ophthalmic ointment (1,000 units per gram) or penicillin solution (5,000 units per milliliter) was started in August, 1954. These preparations were instilled inside the lower lid one time only shortly after birth. One or two drops of the solution or approximately a 1 cm. strip of ointment was used. From September, 1954, to August, 1956, a total of 7,036 infants were given ocular prophylaxis using the penicillin solution or ointment. During the period from Feb. 15, 1955, to Aug. 1, 1956, a careful appraisal was made of each infant's eyes (5,394 newborn infants) at the initial examination in the first 24 hours and again at discharge on the third or fourth day. No significant difference was noted in the number of reactions between aqueous penicillin drops and ophthalmic ointment and therefore, these will be considered as one preparation, hereafter referred to as penicillin ointment. Bacitracin ophthalmic ointment (500 units per gram) was substituted for penicillin ointment in August, 1956. From this time until July 1, 1957, a total of 2,380 infants were given ocular prophylaxis as described above for penicillin. A one-eighth ounce tube of ointment could be used for 25 to 30 newborn infants, and if not used within one week, the tube was discarded. Excessive ointment was not removed from the eyelids.

From February, 1955, to July, 1957, the following procedures and methods of study were carried out.

1. The newborn infants' eyes were examined each day by the pediatric nursing staff and any reaction reported to the pediatrician in charge. Particular note was made of unusual redness or swelling of the eyelids, redness of the conjunctivae, and the nature of any discharges. Cultures were taken frequently at the onset of the study when any degree of inflammation or type of discharge was found. Because many cultures were reported

as showing no growth, subsequent cultures were taken only when an acute inflammation and/or a purulent discharge occurred.

2. The frequency of reactions, classified as to severity and time of onset after birth, were noted and treatment was given after cultures had been taken. Treatment consisted of saline irrigations only in many of the cases particularly in those occurring during the first three days. In those discharges occurring after the third day or if an infection rather than just a reaction was suspected, then bacitracin ophthalmic ointment was used every 3 hours for several days in addition to the saline. All eye infections and reactions cleared within 2 to 4 days on this regime.

3. Each mother was provided with a preaddressed postal card (Fig. 1) when the baby was taken to her. Triweekly lectures were given in which the mothers were advised about the importance of returning the card after two weeks and exactly what information we desired, particularly, in regard to the time of onset and type of inflammation and discharge and how long each lasted. Unfortunately, the return rate of the cards varied from 16 to 69 per cent and averaged only 33 per cent. One reason for this was that some mothers when seen again stated that the infant's eyes had been normal and they forgot to return the card or didn't think it was necessary unless something was wrong.

4. The following criteria were used for classification of the reactions to the ophthalmic ointments. If the eye remained clear for the first four days and then became inflamed or developed a discharge it was considered as a possible infection and *not* as a reaction from the ointment. Reactions to the ophthalmic ointments were classified as follows: (a) minimal—mild redness and swelling of the lids; (b) moderate—moderate swelling, redness, and minimal serous discharge from the eyes; and (c) severe—acute inflammation and a purulent discharge. If the culture was negative in the first four days, this was classified as a reaction; if the culture was positive, it was counted as a reaction and also an infection. This rare reduplication was considered in the final tabulations (Table III).

5. A diagnosis of ophthalmia neonatorum was considered if an acute or hyperacute conjunctivitis occurred at

Parents: Please note any abnormality of the eyes during the first 2 to 3 weeks of life. If a discharge occurs, please note the type of discharge, how long it lasted and what treatment, if any, was used. Have your baby seen by a local doctor or bring him here if any inflammation or discharge occurs.

Condition of Eyes: (Please note whether right or left eye.)

Abnormality Observed:	Age When Noted:	How Long Did It Continue?	What Treatment Was Given?	How Long Was Treatment Given?	Was Treatment Effective?
Right Eye					
Left Eye					

General Condition of Baby in First 2 to 3 Weeks: _____

Birth date: _____ Date Card Sent In: _____

Infant's Name: (First) _____ Name of Your Doctor: _____

(Last) _____ His Address: _____

Fig. 1.—Example of the preaddressed postal card given to each mother before discharge.

any time in the fist two weeks of life whether or not the bacteriologic culture was positive or negative.

RESULTS

During the first eighteen months of the study we observed a low reaction rate to penicillin ointment and in the last eleven months an equally low reaction to the bacitracin ointment. The frequency and degree of ocular reactions to the two ointments are tabulated in Table I. There were no severe reactions and a total of only 1 per cent of mild and moderate reactions for each of the two ointments. The low frequency of reactions was expected since there was only one application of the ointment. The frequency of infections is tabulated in Table II. Gonococcus was not cultured and there were no cases of maternal gonorrheal vaginitis during this period of study. As noted before, the infections were subdivided into two categories: (1) those proved bacteriologically while the patient was in the hospital (well observed in the premature infants); (2) those infants whose eyes remained clear but who developed ocular discharges after the fourth day (the day of discharge) and in whom cultures were not done. This group was evaluated by the postal card returned by the parents and was classified as a possible infection. The infection group contributed a higher number of cases, particularly the possible (not

TABLE I. FREQUENCY AND DEGREE OF OCULAR REACTIONS BETWEEN BACITRACIN AND PENICILLIN OPHTHALMIC OINTMENTS

TYPES OF REACTION TO OINTMENT		MILD	MODERATE	SEVERE	TOTAL
Penicillin (5,394 newborn infants)	Number	50	9	0	59
	Per cent	0.92	0.16	0	1.08
Bacitracin (2,380 newborn infants)	Number	16	5	0	21
	Per cent	0.67	0.21	0	0.88

TABLE II. FREQUENCY OF POSSIBLE (POSTAL CARD REPORT, NO CULTURE) AND PROVED OPHTHALMIC INFECTIONS IN THE NEWBORN INFANT AND TYPES OF BACTERIA CULTURED

		POSSIBLE (NO CULTURE)	PROVED	STAPH. ALBUS	COLIFORM BACILLUS	STAPH. AUREUS	PSEUDOMONAS	PROTEUS	NO GROWTH
Penicillin Ointment (5,394 newborn infants)	Number	168	6	1	2	2	1	0	20
	Per cent	3.1	0.11						0.37
Bacitracin Ointment (2,380 newborn infants)	Number	30	9		7			2	7
	Per cent	1.26	0.37		0.29				0.29

TABLE III. SUMMARY OF OCULAR REACTIONS AND INFECTIONS WHICH OCCURRED DURING THE FIRST TWO WEEKS OF LIFE USING PENICILLIN AND BACITRACIN OPHTHALMIC OINTMENTS

OINTMENT	NEWBORN INFANTS	REACTIONS	INFECTIONS	TOTAL	PER CENT
Penicillin	5394	56	174	230	4.2
Bacitracin	2380	16	39	55	2.3

proved) group. Two factors may account for this: (1) blockage of the nasolacrimal ducts with excessive tears and crusting of the eyelids; (2) misinterpretation by mother of what constituted a purulent discharge, particularly, if there was any edema or a mild nevus flammeus (birthmark) of the lids. The difference in ocular infection rates between the two ointments is not remarkable. It is interesting to note that all of the bacteria obtained in the bacitracin group were gram-negative and that no staphylococci were cultured. These figures are lower than those recently reported[3] (6.6 per cent) for ophthalmia neonatorum. No infant had to be detained in the hospital or readmitted because of an ocular reaction or infection. Table III is a summary of Tables I and II with slight variations due to reduplication (in the first three days) of infections and reactions in a few cases. The frequency of ophthalmia in the bacitracin group was about one half (2.3 per cent) that of the penicillin group (4.2 per cent). This difference is probably not significant since a large part of the ophthalmia was due to the possible infection group.

DISCUSSION

The total number of reactions (including infections) appear to be low when one compares them to other recent reports in which comparison studies were made with erythromycin (10 per cent),[10] Terramycin (4.5 per cent)[13] (5.7 per cent),[14] penicillin (10 per cent),[15] and sodium sulfacetamide (4 per cent).[16] But our figures are higher than those reported for penicillin ointment (0 per cent) by Mallek and others,[2] Allen and others,[17] and by Culler and Clark[8] using Aureomycin drops (0 per cent). This variation is probably due to a difference in the classification of reactions, whether an infection was called a reaction, the period of observation in the hospital, and the duration of observation after discharge. The technique of instilling the ointments or solutions is a major factor, particularly if more than one application is given. The strength of the preparation used must also be considered. Allen[18] has recently pointed out that most of the ophthalmic solution or ointment is washed out of the conjunctival sac within twenty minutes in the normal eye. Considering this factor one wonders if it is of any value to administer one application of an antibiotic or silver nitrate to the newborn infant's eyes in order to prevent an ocular infection, particularly, when gonorrhea conjunctivitis can be treated so effectively with penicillin intramuscularly. As mentioned earlier this danger has decreased greatly in the past decade.

Elliot[19] has pointed out that "sticky eyes" (possible infections) which occur several days after delivery are often due to cross infection between the babies and the staff personnel. And still another cause[14] may be due to mechanical irritations which occur in spite of minute attention given to the technique of cleansing the infant's eyes and applying the prophylactic material. We strongly believe that the best prophylaxis would be to observe carefully the newborn infant's eyes for evidence of infection for several days after delivery without touching or using anything in the eyes at birth. But until definite conclusions can be reached and further evidence is available as to the necessity of using any prophylaxis at all, we should continue

to use a safe, effective, and nonirritating bactericidal ointment in the newborn infant's eyes. It appears that bacitracin ophthalmic ointment fulfills these criteria.

SUMMARY AND CONCLUSIONS

The results of a comparative study of the ocular reactions in the newborn period following the use of penicillin and bacitracin ophthalmic ointments in the prophylaxis of ophthalmic neonatorum are presented. There was no significant difference in the low number of ocular reactions or infections in either group of newborn infants. No serious reaction or infection occurred in a total of 7,774 infants studied. A brief review of the literature is given. It is concluded that bacitracin is a safe, effective and nonirritating bactericidal ophthalmic ointment for ophthalmia neonatorum prophylaxis, but that the ideal approach at this time would be to observe the eyes closely and use no prophylaxis at all.

Acknowledgment is due to Julian Love, Captain (MC) USN Ret., former Commanding Officer, J. M. Jordan, Captain (MC) USN, Chief of Ophthalmology, for their kind advice during the course of this study and to the newborn nursing staff and particularly to Miss M. Hastings, R.N.

REFERENCES

1. Ormsby, H. L.: Ophthalmia Neonatorum, Canad. M. A. J. **72**: 576, 1955.
2. Mallek, H., Spohn, R., and Mallek, Josephine: On the Comparative Use of Silver Nitrate and Penicillin in the Eyes of the Newborn, Canad. M. A. J. **68**: 117, 1953.
3. Society Proceedings: Ophthalmia Neonatorum Prophylaxis, Round Table Conference on Ocular Therapeutics, Am. J. Ophth. **39**: 87, 1955.
4. Meleney, F. L., and Johnson, B. A.: A Review of Systemic Bacitracin Therapy, U. S. Armed Forces M. J. **6**: 834, 1955.
5. Jawetz, E.: Antimicrobial Therapy, Polymixin, Neomycin, and Bacitracin, Pediat. Clin. North America **2**: 329, 1956.
6. Taylor, Mary D., and Calman, R. M.: The Care of the Eyes at Birth, J. Obst. & Gynaec. Brit. Emp. **55**: 642, 1948.
7. Leff, M.: The Care of the Eyes in the Newborn, West. J. Surg. **59**: 176, 1951.
8. Culler, A. M., and Clark, S. G.: Aureomycin as Prophylaxis Against Ophthalmia Neonatorum, Am. J. Ophth. **34**: 982, 1951.
9. Schultz, K. W., and Hartmann, A.: Critical Remarks on Penicillin Blennorrhea Prophylaxis in the Newborn, Deutsche med. Wchnschr. **79**: 1631, 1954.
10. Wachter, H. E., and Pennoyer, M. M.: Prophylaxis in the Eyes of Newborn Infants, Missouri Med. **53**: 187, 1956.
11. Editorial: Ophthalmia Neonatorum Prophylaxis, J. PEDIAT. **50**: 789, 1957.
12. Lehrfeld, L.: Prevention of Blindness in the Newborn, Correspondence, J. A. M. A. **143**: 1360, 1950.
13. O'Brien, D.: Terramycin in the Prophylaxis of Ophthalmia Neonatorum, Lancet. **1**: 347, 1952.
14. Kozinn, P. J., Minsky, A., and Solomons, E.: Oxytetracycline Ophthalmic Solution in the Prophylaxis of Ophthalmia Neonatorum, Antibiotics Annual edit. Welch, H., and Marti-Ibaney, F., New York, 1955-56, Medical Encyclopedia, Inc., p. 307.
15. Davidson, H. H., Hill, Justina H., and Eastman, N. J.: Penicillin in the Prophylaxis of Ophthalmia Neonatorum, J. A. M. A. **145**: 1052, 1951.
16. Bickel, J. E.: Sodium Sulfacetamide For the Prophylaxis of Gonorrheal Ophthalmia Neonatorum, J. PEDIAT. **37**: 854, 1950.
17. Allen, J. H., and Barrere, L. E.: Prophylaxis of Gonorrheal Ophthalmia of the Newborn, J. A. M. A. **141**: 522, 1949.
18. Allen, J. H.: Ocular Bacteriology (Motion Picture) New York, 1955, Medical Film Guild.
19. Elliot, R. A.: Ophthalmic Neonatorum: Review of Prophylactic Methods at Present in Use, Month. Bull. Min. Health **11**: 135, 1952.

FORMATION OF MUCOUS MEMBRANE LESIONS SECONDARY TO PROLONGED USE OF ONE PER CENT AQUEOUS GENTIAN VIOLET

EUGENE L. SLOTKOWSKI, M.D.
CHICAGO, ILL.

THE use of 1 per cent aqueous solution of gentian violet in the treatment of oral thrush in the neonatal period and early infancy is an accepted procedure. Other than discoloration of the tissues, gentian violet is believed to be a safe and harmless medication. Although thrush is said to be a self-limited disease, as a rule, a 1 per cent aqueous solution of gentian violet is prescribed.

The purpose of this paper is to point out that the application of a 1 per cent aqueous solution of gentian violet to the mucous membranes of the infant in the management of thrush is not without danger. Prolonged use of this medication may result in the formation of mucous membrane lesions.

CASE REPORT

The infant was first seen at a U.S. Army Hospital on Dec. 19, 1955, at approximately 8 weeks of age. Thrush had been diagnosed at another military installation on the eighth day of life, and gentian violet, to be administered twice daily, was prescribed. After an unspecified period of time the use of gentian violet was increased to three times a day. The patient was seen again at 3 weeks of age, and the mother was instructed to continue use of gentian violet. At 6 weeks of age the infant was re-examined, and the mother reported that there was some improvement. She was advised to continue gentian violet treatments three times a day until she reached the next military installation.

Physical examination revealed a normal 8-week-old infant with brownish patches, gelatinous-like in appearance, on the right buccal mucosa near the mandibular maxillary junction (Fig. 1). Similar lesions were present on the undersurface of the tongue. Lesions measuring 3 to 5 mm. in size were noted on the hard and soft palates. Smear and culture were negative for Monilia.

After gentian violet applications were discontinued, the lesions healed rapidly and have not recurred.

Fig. 1.—Appearance of mucous membranes after application of 1 per cent aqueous solution of gentian violet for a period of six weeks. Note lesions on buccal mucosa and palate; gelatinous-like lesions on undersurface of tongue are not visible in photograph.

DISCUSSION

Thrush is seen more frequently in premature and weak or debilitated infants than in healthy term infants.

According to Grulee and Eley,[1] trauma to mucous membranes of the mouth may be a predisposing factor. However, the majority of newborn infants who develop the disease are otherwise well and show no evidence of injury to the mucous membranes.

It has been stated[2] that there is no effective treatment for Candida infections, that thrush is usually benign, and that the process subsides in a few days or weeks, spontaneously or coincidentally, with the application of gentian violet, Zephiran, or hydrogen peroxide. Nelson[3] states that oral thrush in an otherwise healthy infant is usually a self-limited infection. Holt[4] feels that local treatment is not essential but recovery can be accelerated by the use of a mild antiseptic. Some authors[5, 6] take a different view as to the potential danger of thrush in the newborn period, claiming that if the infant is healthy the thrush remains localized to the buccal mucous membranes; however, in debilitated infants it may spread to involve the gastrointestinal tract and even prove fatal.

Gentian violet is recommended by various authors for the treatment of thrush in the newborn period. Grulee and Eley recommend a 1 or 2 per cent solution; Hughes[7] and Holt[4] recommend a 1 per cent solution. Monerief[8] prefers a ½ per cent solution of gentian violet. It is generally agreed that the initial treatment should be given twice daily; later a single daily application will suffice. There is no comment in any of the standard pediatric textbooks that prolonged topical application of gentian violet is potentially dangerous or may cause local irritation.

In several instances—personally observed—application of gentian violet for a prolonged period of time resulted in the formation of irritative, ulcerative, or gelatinous-like lesions. The buccal mucosa and the undersurface of the tongue were the areas most frequently involved. With the appearance of these new lesions, the infant apparently has a great deal of tenderness of the mouth, with gagging and choking upon feeding. Since these cases were believed to represent resistant thrush, the use of gentian violet was continued; as a matter of fact, it was applied more frequently. Finally, after the medication was discontinued, the lesions cleared rapidly.

In a recent case report[9] there is some question as to whether gentian violet irritation had not been superimposed on the original pathology.

This particular infant weighed 4 pounds 11 ounces and was discharged on the tenth day of life. A few hours later he was examined at home and a white tongue typical of oral moniliasis was found. One per cent aqueous gentian violet solution was applied to the mouth and tongue as prescribed (the authors do not mention the frequency of application). Ten days later there was no improvement of the mouth or tongue and a 2 per cent aqueous solution of ferric chloride was ordered as a substitute for the gentian violet. Two days later the undersurface of the tongue, soft palate, gums, and posterior pharynx showed extensive involvement. Several ulcerated and bleeding areas were present on the tongue, and edema was severe. The infant was admitted to the hospital. Culture failed to reveal Monilia. (It seems unusual that cultures should be negative in the presence of the extensive local pathology described by the authors.) X-rays of

the chest confirmed the presence of pneumonia.

Improvement followed administration of Mycostatin, penicillin, streptomycin, and Gantrisin. Within forty-eight hours edema and bleeding completely disappeared from the mouth. (One cannot help but wonder whether the improvement in the local pathology resulted from the Mycostatin or the fact that topical gentian violet had been discontinued.)

SUMMARY

The possibility of forming mucous membrane lesions following prolonged use of gentian violet must be kept in mind. If the monilial infection does not respond in a reasonable length of time, discontinuing gentian violet should be seriously considered.

REFERENCES

1. Grulee, C. G., and Eley, R. C.: The Child in Health and Disease, ed. 2, Baltimore, 1952, Williams & Wilkins Co.
2. Winter, W. D., Jr.: Candida (Monilia) Infections in Children, Pediat. Clin. North America, Feb. p. 151, 1955.
3. Nelson, W. E.: Textbook of Pediatrics, ed. 6, Philadelphia, 1954, W. B. Saunders Co.
4. Holt, L. E., Jr., and McIntosh, R.: Holt Pediatrics, ed. 12, New York, 1953, Appleton-Century-Crofts.
5. Crosse, V. M.: The Premature Baby, ed. 3, Philadelphia, 1952, The Blakiston Co.
6. Ludlam, G. B., and Henderson, J. L.: Neonatal Thrush in a Maternity Hospital, Lancet 1: 64, 1942.
7. Hughes, J. G.: Pediatrics in General Practice, ed. 1, New York, 1952, McGraw-Hill Book Co., Inc.
8. Moncrief, A., and Evans, P.: Diseases of Children, ed. 5, London, 1953, Williams & Wilkins Co.
9. Beckmann, A. J., and Navarro, J. E.: Pneumonia Complicating Oral Thrush Treated With Mycostatin, a New Antifungal Antibiotic, J. PEDIAT. 46: 587, 1955.

Mary Ropes died January 15, 1796. "Dropsy in the head, aet. 11. The physicians agreed upon this case."

BENTLY'S DEATHS IN EAST CHURCH, SALEM.

NOVOBIOCIN IN COMMON PEDIATRIC INFECTIONS

ANGELLA D. FERGUSON, M.D., GERTRUDE C. TEIXEIRA, M.D., AND ROLAND B. SCOTT, M.D.
WASHINGTON, D.C.

ACCORDING to reports dealing mainly with adult patients,[1-4] novobiocin has been found to be highly effective against infections caused by *Micrococcus pyogenes* (staphylococcus). Many of the strains of this organism are resistant to other antibiotics. The purpose of this study was to evaluate the drug clinically in the treatment of acute infections in children and to determine the blood concentration of novobiocin after a single oral dose. Both the sodium and the calcium salts of novobiocin were administered and compared in this study.

METHOD OF STUDY

Fifty-six children with common childhood infections were used in this study, all under 12 years of age. Forty-seven of these children were treated with the sodium salt and 9 received the calcium salt of novobiocin (Tables I and II). Of the patients who received the sodium salt of novobiocin, 19 were hospitalized, and 28 were treated in the outpatient department. All patients who received the calcium preparation of the drug were hospitalized.

The dosage used was 20 mg. of novobiocin orally per kilogram of body weight per day in divided doses every 6 hours. Children who had received other antibiotic or chemotherapeutic agents were not used in this study.

Before and after administration of the drug the following studies were obtained: hemogram, urinalysis, nose and throat culture, blood culture as indicated, and liver function studies including serum bilirubin, total protein, alkaline phosphatase, icteric index, cholesterol, and cephalin flocculation. Serum novobiocin determinations were performed on all hospitalized patients at specified intervals, after the drug was administered.

In order to determine the blood concentration of the drug after a single oral dose, 4 patients were given the sodium salt and 8 were given the calcium salt of novobiocin. Serial blood concentrations of novobiocin were obtained at specified intervals (Tables III and IV).

RESULTS

Clinical Evaluation of Sodium Salt of Novobiocin.—Of the 19 hospitalized patients treated with the sodium salt of novobiocin, 10 had pneumonia and 9 had bronchitis or other upper respiratory tract infections. Pertinent clinical and laboratory data are presented in Table I. A composite graph of the temperature responses of the patients

From the Department of Pediatrics, Howard University College of Medicine and the Pediatrics Service of Freedmen's Hospital, Washington, D. C.

The novobiocin was supplied as Cathomycin through the courtesy of Dr. David S. Brashear of the Research Laboratories of Merck Sharp & Dohme, West Point, Pa.

TABLE I. SUMMARY OF CLINICAL DATA ON HOSPITALIZED PATIENTS TREATED WITH SODIUM SALT OF NOVOBIOCIN

NO.	AGE	CLINICAL DIAGNOSIS	DURATION OF SYMPTOMS BEFORE DRUG	CATHOMYCIN DOSAGE: TOTAL DOSE PER DAY (MG.)	BLOOD LEVEL MEQ./C.C.: 24 HR.	BLOOD LEVEL MEQ./C.C.: 36 HR.	FEVER: MAXIMUM ELEVATION (° F.)	FEVER: DURATION	DURATION OF TREATMENT (DAYS)	BACTERIOLOGY: SOURCE	BACTERIOLOGY: ORGANISM
1.	4 yr.	(1) Bronchopneumonia (2) Acute follicular tonsillitis	24 hr.	240	15.21	12.36	100.2	24 hr.	4	(1) Blood (2) Nose (3) Throat	No growth Alpha streptococcus Neisseria species Alpha streptococcus *Micrococcus pyogenes* var. *aureus*
2.	3 mo.	(1) Bronchopneumonia (2) Tracheobronchitis	1 wk.	120	8.81	7.23	102.0	1 day	8	(1) Nose (2) Throat	Neisseria species *M. pyogenes* var. *albus* Diphtheroids Alpha streptococcus *M. pyogenes* var. *albus* Lactobacillus species
3.	2 yr.	(1) Bronchopneumonia (2) Otitis media (3) Tonsillitis	2 days	200	10.14	9.23	103.0	48 hr.	8	(1) Blood (2) Nose (3) Throat	No growth *M. pyogenes* var. *aureus* Alpha streptococcus
4.	3 yr.	(1) Bronchopneumonia (2) Tonsillitis	3 days	300	11.45	12.20	106.0	36 hr.	6	(1) Blood (2) Nose (3) Throat	No growth Alpha streptococcus *M. pyogenes* var. *aureus* Alpha and beta streptococci
5.	6 yr.	Acute follicular tonsillitis	24 hr.	400	20.01	24.00	102.4	3 days	6	(1) Blood (2) Nose (3) Throat	No growth *M. pyogenes* var. *albus* Alpha streptococcus *M. pyogenes* var. *albus* Alpha streptococcus
6.	3 yr.	Acute follicular tonsillitis	24 hr.	320	21.3	18.26	104.8	36 hr.	5	(1) Blood (2) Nose (3) Throat	No growth *M. pyogenes* var. *aureus* Alpha streptococcus Neisseria species

7.	5 mo.	Bronchopneumonia	5 days	136	12.07	11.27	102.4	72 hr.	6	(1) Blood (2) Nose (3) Throat	No growth Alpha streptococcus Neisseria species *Escherichia coli;* alpha and beta streptococcus *Diplococcus pneumoniae*
8.	9 mo.	(1) Bronchopneumonia (2) Otitis media (3) Tonsillitis	4 days	200	15.52	12.04	104.4	5 days	8	(1) Blood (2) Nose (3) Throat	No growth *M. pyogenes* var. *aureus* Alpha streptococcus *D. pneumoniae*
9.	8 yr.	Acute membraneous tonsillitis	7 days	500	21.01	17.21	104.0	2 days	8	(1) Blood (2) Nose (3) Throat	No growth Beta streptococcus Neisseria species *E. coli* Beta streptococcus Neisseria species
10.	6 mo.	Tracheobronchitis	2 wk. (?)	160	8.21	10.01	104.0	72 hr.	6	(1) Blood (2) Nose (3) Throat	No growth *M. pyogenes* var. *aureus* Neisseria species *D. pneumoniae* Beta streptococcus *M. pyogenes* var. *aureus*
11.	5 yr.	(1) Cellulitis of leg (2) Otitis media (3) Pharyngitis	1 wk.	500	21.05	18.21	101.0	24 hr.	6	(1) Blood (2) Nose (3) Throat	No growth *M. pyogenes* var. *aureus* *E. coli* *M. pyogenes* var. *aureus*
12.	16 mo.	Early bronchopneumonia	3 wk. (?)	280	14.01	11.32	102.0	24 hr.	5	(1) Blood (2) Nose (3) Throat	No growth Alpha streptococcus Neisseria and Paracolon species Alpha streptococcus Neisseria species *D. pneumoniae* Paracolon species
13.	2½ yr.	(1) Otitis media (2) Nasopharyngitis	48 hr.	260	17.82	10.01	100.4	12 hr.	5	(1) Nose (2) Throat	Neisseria species *M. pyogenes* var. *aureus* Alpha streptococcus Beta streptococcus *D. Pneumoniae* Alpha streptococcus

TABLE I—CONT'D

NO.	AGE	CLINICAL DIAGNOSIS	DURATION OF SYMPTOMS BEFORE DRUG	CATHOMYCIN DOSAGE: TOTAL DOSE PER DAY (MG.)	BLOOD LEVEL MCG./ML.: 24 HR.	BLOOD LEVEL MCG./ML.: 36 HR.	FEVER: MAXIMUM ELEVATION (° F.)	FEVER: DURATION	DURATION OF TREATMENT (DAYS)	BACTERIOLOGY: SOURCE	BACTERIOLOGY: ORGANISM
14.	13 mo.	Tonsillopharyngitis	1 wk.	200	7.62	11.04	100.0	72 hr.	4	(1) Nose (2) Throat	*E. coli* Alpha and beta streptococci *M. pyogenes* var. *aureus* Neisseria species
15.	14 mo.	(1) Tonsillopharyngitis (2) Upper respiratory infection (3) Chronic otitis media with perforated drum (4) Fracture of right femur	1 wk.	260	10.02	9.98	100.0	24 hr.	4	(1) Nose (2) Throat (3) Ear	Neisseria species Alpha and beta streptococci *M. pyogenes* var. *aureus* *M. pyogenes* var. *aureus* *E. coli*
16.	19 mo.	Lobar pneumonia	2 wk. (?)	280	22.00	17.32	102.0	24 hr.	7	(1) Blood (2) Nose (3) Throat	*M. pyogenes* var. *aureus* *M. pyogenes* var. *aureus* Beta streptococcus Diphtheroids
17.	8 mo.	(1) Bronchopneumonia (2) Tonsillopharyngitis	3 days	160	21.45	11.32	102.0	3 days	6	(1) Nose (2) Throat	*M. pyogenes* var. *aureus* Alpha streptococcus *D. pneumoniae* Alpha and beta streptococcus *D. pneumoniae*
18.	1½ yr.	Bronchopneumonia	4 days	280	7.34	14.00	99.8	—	4	(1) Nose (2) Throat	*M. pyogenes* var. *aureus* Alpha and beta streptococcus *D. pneumoniae*
19.	4 yr.	(1) Acute follicular tonsillitis (2) Acute pharyngitis (3) Acute rhinitis	6 days	400	19.02	17.34	102.0	24 hr.	5	(1) Nose (2) Throat	*D. pneumoniae* *M. pyogenes* var. *aureus* Alpha and beta streptococcus

having pneumonia is shown in Fig. 1. The average duration of fever in those cases with pneumonia was 27.6 hours. Representative cases are given here.

In the group of patients having upper respiratory tract infections, the average duration of fever was 22 hours. A typical case is presented below.

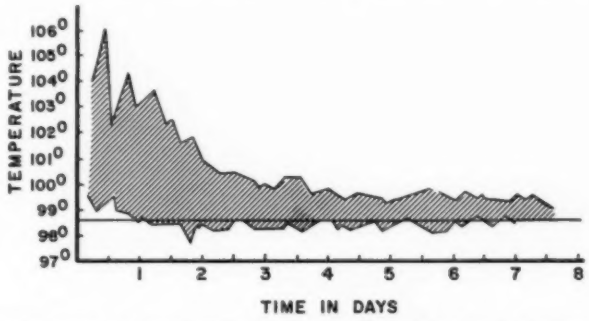


Fig. 1.—Composite graph of temperature curves of 10 patients with pneumonia who were treated with the sodium salt of novobiocin.

CASE REPORTS

CASE 1.—E. E., a 9-month-old Negro girl, entered the hospital Oct. 23, 1956, with a history of fever of 4 days' duration and hemoptysis on the day of admission. X-ray confirmed a clinical diagnosis of bronchopneumonia. A blood culture was negative, but nose and throat cultures revealed pneumococci and alpha and beta streptococci. The patient was given 20 mg. per kilogram per day of the sodium salt of novobiocin, orally (50 mg. every 6 hours) for 8 days. Temperature was normal on the second hospital day, and the chest had cleared in 4 days.

CASE 2.—A. A., a 5-month-old Negro boy, entered the hospital Oct. 8, 1956, with a history of a cold for 5 days, vomiting for 4 days, and dyspnea for 1 day. The clinical diagnosis of bronchopneumonia was confirmed by x-ray. No growth was obtained from the blood culture but nose and throat cultures revealed *Micrococcus pyogenes* var. *aureus* and *pneumococcus*. The patient received 20 mg. per kilogram per day of sodium salt of novobiocin (35 mg. every 6 hours) for 6 days. The temperature was normal after 72 hours, and the chest was clear on the sixth day.

CASE 3.—L. G., an 8-year-old Negro girl, was admitted Oct. 16, 1956, with a complaint of anorexia, fever, and sore throat of one week's duration. On admission, the temperature was 104° F., the breath had a foul odor, and the tonsils were large, beefy red, and were covered by patches of mucopurulent exudate. Blood cultures were negative, but nose cultures revealed alpha streptococci and *M. pyogenes* var. *aureus* and throat culture grew alpha and beta streptococci and Neisseria species. The patient was placed on 20 mg. per kilogram per day of the sodium salt of novobiocin (125 mg. every 6 hours) for 8 days. Fever subsided and remained normal after the second hospital day. The tonsils returned to normal appearance by the seventh day.

Of the 28 patients treated in the outpatient department, all gave an excellent response to the drug except one. The following diagnoses were made: nasopharyngitis, 5; tonsillopharyngitis, 14; otitis media, 6; bronchopneumonia, 6; bronchitis, 2; and gastroenteritis, 3. The one patient who did not respond to novobiocin had

TABLE II. SUMMARY OF CLINICAL DATA ON HOSPITALIZED PATIENTS TREATED WITH CALCIUM SALT OF NOVOBIOCIN

NO.	AGE	CLINICAL DIAGNOSIS	DURATION OF SYMPTOMS BEFORE DRUG (DAYS)	CATHOMYCIN CALCIUM* TOTAL DOSE PER DAY (MG.)	BLOOD LEVEL AFTER INITIAL DOSE MCG./ML.	UNTOWARD REACTION	FEVER MAXIMUM ELEVATION (° F.)	FEVER DURATION	DURATION OF TREATMENT (DAYS)	BACTERIOLOGY SOURCE	BACTERIOLOGY ORGANISM
1.	8 yr.	(1) Tonsillopharyngitis (2) Bronchopneumonia	4	500	4-hr. level 38.21	None	103.6	4 days	7	(1) Blood (2) Nose (3) Throat	No growth Alpha streptococcus Neisseria species *M. pyogenes* var. *albus* Alpha streptococcus *M. pyogenes* var. *albus*
2.	2½ yr.	(1) Bronchitis (2) Otitis media	8	280	3-hr. level 41.02	None	101.8	2 days	6	(1) Blood (2) Nose (3) Throat	No growth Alpha and beta streptococci Paracolon and Neisseria species Alpha streptococcus *M. pyogenes* var. *aureus*
3.	13 mo.	(1) Pharyngitis (2) Early bronchitis	4	200	4-hr. level 22.42	Vomited first 2 doses	102.8	72 hr.	2	(1) Blood (2) Nose and throat (3) Stool	No growth *M. pyogenes* var. *aureus* Alpha streptococcus *D. pneumoniae* *E. coli* *M. pyogenes* var. *aureus*
4.	4 yr.	(1) Acute pharyngitis (2) Impetigo—localized to lip (3) Purulent rhinitis	10	400	4-hr. level 52.41	None	101.6	2 days	7	(1) Blood (2) Nose (3) Throat	No growth *M. pyogenes* var. *aureus* *M. pyogenes* var. *aureus*

5.	6 yr.	Tonsillopharyngitis	3	400	4-hr. level 30.01	None	100.8	12 hr.	4	(1) Nose (2) Throat	Alpha and beta streptococci Neisseria species *M. pyogenes* var. *aureus* *D. pneumoniae* Alpha streptococcus
6.	1½ yr.	Bronchopneumonia	5	280	3-hr. level 20.38	None	104.6	4 days	9	(1) Blood (2) Nose (3) Throat	No growth Alpha and beta streptococci *M. pyogenes* var. *aureus* *M. pyogenes* var. *aureus* Alpha streptococcus *D. pneumoniae*
7.	3 yr.	Tonsillopharyngitis	3	320	2-hr. level 41.82	None	101.8	2 days	5	Nose and throat	*M. pyogenes* var. *aureus* Alpha streptococcus *E. coli*
8.	2 yr.	(1) Acute follicular tonsillitis (2) Sinusitis	4	200	2-hr. level 27.62	None	103.8	3 days	7	Nose and throat	*M. pyogenes* var. *aureus* Beta streptococcus Lactobacillus species
9.	8 yr.	(1) Bilateral otitis media (2) Pharyngotonsillitis	7	500	3-hr. level 29.38	None	102.4	36 hr.	7	Nose and throat	*M. pyogenes* var. *aureus* Alpha streptococcus

*Twenty milligrams per kilogram per day.

bronchopneumonia and acute gastroenteritis. Alpha streptococci and *E. coli* were isolated from the nose and throat, and *E. coli* was obtained from the stool.

Clinical Evaluation of Calcium Salt of Novobiocin.—Nine patients were treated with the calcium salt of novobiocin. In this group of patients, fever subsided after an average of 17.8 hours. Other pertinent laboratory and clinical data are presented in Table II.

Serum Novobiocin Levels After a Single Oral Dose.—Single oral doses of novobiocin were administered to 12 subjects, and blood samples were taken in order to determine the concentration of the drug (Tables III and IV).

COMMENT

The efficiency of novobiocin has been established in the treatment of a variety of common bacterial infections in childhood. A satisfactory clinical and laboratory response was noted in all

TABLE III. BLOOD LEVELS EXPRESSED IN MICROGRAMS PER MILLILITER OF SERUM FOLLOWING A SINGLE ORAL DOSE OF THE SODIUM SALT OF NOVOBIOCIN

	2 HOURS (MCG. %)	4 HOURS (MCG. %)	6 HOURS (MCG. %)	12 HOURS (MCG. %)	24 HOURS (MCG. %)
Case 1	5.7	10.45	11.14	9.82	8.34
Case 2	2.83	9.35	14.98	10.54	9.31
Case 3	7.81	12.07	10.42	6.02	7.30
Case 4	6.01	11.20	15.11	14.23	12.09

The amount of drug given was one-fourth the recommended daily total dosage, i.e., 5 mg. per kilogram.

TABLE IV. BLOOD LEVELS EXPRESSED IN MICROGRAMS PER MILLILITER OF SERUM FOLLOWING A SINGLE ORAL DOSE OF THE CALCIUM SALT OF NOVOBIOCIN

SUBJECT	HOURS AFTER NOVOBIOCIN CALCIUM	BLOOD LEVEL (MCG./ML.)	DOSAGE (MG.)
1 S. L.	4	45.45	250
	6	19.10	
2 M. T.	4	31.14	250
	6	12.02	
3 E. D.	2	41.38	250
	4	29.54	
	6	9.83	
4 L. H.	2	51.81	250
	4	34.01	
	6	11.82	
5 S. M.	4	52.94	250
	6	24.74	
6 S. S.	3	65.38	50
	5	42.78	
7 J. M.	2	39.0	250
	4	27.78	
	6	17.14	
8 J. M. (repeat)	1	57.12	250
	3	29.10	
	5	21.78	

The amount of drug given was one-fourth the recommended daily total dosage, i.e., 5 mg. per kilogram.

patients treated with the drug except one infant treated in the outpatient department. Although the serum concentrations of novobiocin were all substantial, higher levels were obtained with the calcium salt than with the sodium salt. The latter derivative, however, seemed to be more palatable and hence more acceptable to the children. This drug will probably find its greatest area of usefulness in the treatment of staphylococcal infections which are resistant to the older antibiotics.

SUMMARY

Fifty-six patients with common childhood infections were treated with novobiocin. A good response to the drug was obtained in all patients except one infant treated in the outpatient department. There were no toxic or untoward reactions observed. Higher blood levels were obtained with the calcium salt than with the sodium salt of novobiocin. The drug was well absorbed following oral administration.

REFERENCES

1. Martin, W. J., Heilman, F. R., Nichols, D. R., Wellman, W. E., and Geraci, J. E.: (Streptonivicin Cathomycin): A New Antibiotic—Preliminary Report, Proc. Staff Meet. Mayo Clin. **30**: 540, 1955.
2. Feng, K. L., and Cariell, L. L.: Novobiocin, a Laboratory and Clinical Evaluation, Antibiotic Medicine **2**: 268, 1956.
3. Martin, W. J., Heilman, F. R., Nichols, D. R., Wellman, W. E., and Geraci, J. E.: Novobiocin (Streptonivicin Cathomycin): Further Observations, Proc. Staff Meet. Mayo Clin. **31**: 416, 1956.
4. Martin, W. J., Heilman, F. R., Nichols, D. R., Wellman, W. E., and Geraci, J. E.: Novobiocin for Infections Due to Micrococcus Pyogenes, J. A. M. A. **162**: 1150, 1956.

APPARENT SENSITIZATION TO NOVOBIOCIN

Case Report

James G. Hughes, M.D.
Memphis, Tenn.

The introduction of new antibiotics into the therapeutic armamentarium is invariably followed by instances of toxic reactions, sensitization phenomena, development of resistant bacterial strains, and dangers of superinfection. These are the inherent penalties of therapeutic progress.

It is the purpose of this paper to present the case of a child thought to have had a severe allergic reaction to novobiocin, which, in several respects, resembled the Stevens-Johnson syndrome. A striking feature of the case was involvement of the nervous system, with nuchal rigidity, marked irritability, stupor, pleocytosis of the cerebrospinal fluid, but negative bacterial and viral studies. Since novobiocin is a relatively new antibiotic, it is thought that a brief report of this case may be of interest. No attempt will be made to review the frequency and clinical manifestations of sensitivity to this drug.

CASE REPORT

B. B., a 7-month-old white male infant weighing 7 kilograms, was admitted to the Le Bonheur Children's Hospital, Dec. 19, 1956. On December 4 he had contracted a respiratory infection of moderate degree accompanied by hoarseness and cough. His local physician prescribed a preparation of novobiocin (Albamycin) in dosage of 125 mg. orally three times a day for four days. Hoarseness diminished but the cough persisted. He had been given this drug in November because of an upper respiratory infection.

On December 11, three days after the last course of novobiocin was discontinued, the infant developed marked irritability and fever. Two days later he was admitted to a hospital in Mississippi because of increasing irritability, fever, and sudden development of a rash involving the skin of the legs and arms, consisting of red macules 1 to 2 mm. in diameter. The appearance of the rash and the presence of postauricular lymph node enlargement led the physician to suspect rubella as the probable diagnosis. However, this diagnosis was rapidly abandoned when on the same day (five days after discontinuance of novobiocin) the child developed raw red spreading lesions about the lips and a severe inflammation of the mucosa of the mouth and tongue. The previously mentioned rash on the legs and arms now had extended to involve the skin of the chest and neck.

The highly inflamed lips rapidly cracked and the inflammation of the mouth assumed a thrushlike appearance. Hoarseness, moderate sternal retraction, and scattered râles and rhonchi were now apparent.

On December 13 a roentgenogram of the chest was normal. Therapy with nebulization of water in a Croupette, and 125 mg. of oxytetracycline orally every six hours, was instituted.

From the Division of Pediatrics, University of Tennessee, and the Le Bonheur Children's Hospital, Memphis.

Cultures obtained from the mouth and throat at this time were positive for beta hemolytic streptococci, pneumococci, and *Candida albicans*. The white blood cell count was 23,000 per cubic millimeter, with a differential count of 41 per cent polymorphonuclears, 53 per cent lymphocytes, 5 per cent monocytes, and 1 per cent eosinophils. The hemoglobin was 10 grams per 100 c.c.

On December 14 the cerebrospinal fluid was clear but contained 186 white blood cells per cubic millimeter, 94 per cent of which were lymphocytes and 6 per cent polymorphonuclears. The glucose content of the cerebrospinal fluid was 66 mg. per cent and the protein 41.4 mg. per cent. Smears and cultures for bacteria were negative. Studies to identify viral agents were also negative.

The severe illness continued unabated. The leukocytosis persisted, the white blood cell count ranging between 16,000 and 27,000 per cubic millimeter. The urinalysis remained normal.

On December 19 the child was admitted to the Le Bonheur Children's Hospital. Examination revealed an extremely irritable, acutely ill, whining, fretting infant who whimpered constantly, especially when handled. The hands and feet were edematous and had a dusky-pink color, particularly noted in the fingers, toes, and nails. These areas blanched when pressed upon, and then the dusky color slowly returned in the blanched areas. The child cried excessively when his hands and feet were handled.

The lips and oral mucosa were extremely red, shiny, and somewhat glazed. Excoriations were present over the knees, probably from restlessly rubbing against the bedclothes. A few pink macular lesions were noted on the trunk and extremities.

The eardrums were normal, as were the conjunctivae and the mucosa of the nasal passages. There was no inflammation near the urethral meatus or anus. There was inspiratory retraction of the sternum, apparently due to a mild pectus cavum. The heart and lungs were normal to examination, as was the abdomen. There was no enlargement of the liver or spleen and no masses were palpated in the abdomen.

Neurologic examination revealed evidence of mild left facial weakness, the mouth drawing to the right when the infant cried and the right eye closing more tightly than the left. Nuchal rigidity was absent on admission but present the next day. The patellar reflexes were hyperactive, but the Kernig and Brudzinski signs were negative. Abdominal reflexes were absent.

The admission routine blood count revealed a hemoglobin of 14.7 grams per 100 c.c., a red blood cell count of 5,010,000 per cubic millimeter, and a white blood cell count of 17,350 per cubic millimeter. The differential count showed 48 per cent polymorphonuclears, 1 per cent eosinophils, 45 per cent lymphocytes, and 6 per cent monocytes. Toxic granulations were noted in the neutrophils. The thrombocytes were adequate in number. The voided urine was clear in appearance, acid in reaction, contained a faint trace of protein, was negative for sugar, and had 5 to 10 leukocytes and rare red blood cells per high-power field.

On admission the cerebrospinal fluid was clear, colorless, and contained 16 leukocytes per cubic millimeter, of which 15 were lymphocytes and 1 was a polymorphonuclear. The protein content was 19 mg. per cent and the sugar 69 mg. per cent. Cultures of the cerebrospinal fluid and blood were negative. The carbon dioxide combining power was 21 meq. per liter. A culture from the oral lesions revealed the predominating organism to be *B. proteus*. The cephalin flocculation test was negative. A chest roentgenogram was normal.

Treatment and Clinical Cause.—The illness was managed without the use of any drugs other than phenobarbital for restlessness, bland ointments to the

skin, and hydrocortisone. The dose of hydrocortisone was 50 mg. every six hours intramuscularly for two days, 25 mg. every six hours for one day, and 12.5 mg. every six hours for the next day. The cortisone was started two days after admission, during which time there had been difficulty in establishing the diagnosis.

There was a rapid and gratifying response to steroid therapy. The skin lesions and edema began to recede steadily and the fever was reduced from 103.6° F. to normal within three days. However, he developed new lesions on the soles of the feet, consisting of small nodules which were discrete and firm and had a reddish color.

The most notable clinical feature was excessive irritability. Although stiffness of the neck and back had not been noted on admission, it was thought to be present the next day, perhaps contributed to in part by the lumbar puncture that had been performed. A mild diarrhea developed, which subsided within a few days.

He was discharged to the care of his local physician one week after admission to the Le Bonheur Children's Hospital. The doses of cortisone were tapered gradually and he made an apparently complete recovery.

COMMENTS AND DISCUSSION

This case is presented as a probable example of extreme sensitization to novobiocin in a 7-month-old infant who had had one previous course of the drug. The chief features suggesting an allergic response to the administration of the drug were: severe edema of the hands and feet, fingers and toes; marked pain on handling of the hands and feet, interpreted to represent allergic reaction in the small joints; the presence of a rather generalized erythematous rash which did not fit any category of rashes of contagious diseases; extremely severe inflammation of the mucous membrane of the mouth; and dramatic, rapid improvement when hydrocortisone therapy was instituted.

It is possible that pleocytosis in the cerebrospinal fluid was the result of a similar allergic reaction in the central nervous system which also accounted for the severe mental and emotional changes, so striking in this patient's illness. The child was disoriented and semicomatose for the first few days of hospitalization.

Careful consideration was given to the possibility of the Stevens-Johnson syndrome, but there were several features about the case which failed to match observations noted in outspoken instances of this syndrome in other patients seen in this center.

This case was clearly not one of viral encephalitis, because of the extensive changes in the mucous membrane, skin, soft tissues, and joints, and negative viral studies.

It is believed that the finding of *Candida albicans* represented a secondary infection superimposed on an already damaged oral mucosa.

It is recognized that proof that this patient's severe illness was caused by extreme sensitivity to novobiocin would require readministration of the drug, followed by observation of allergic response or, perhaps, demonstration of intradermal sensitization. Considering the gravity of the child's illness, this was considered too dangerous. The possibility of retesting at a later date with a small dose of novobiocin was discussed with the parents, but, as would be expected, they rejected the idea.

THE ROENTGENOGRAPHIC DIAGNOSIS OF GEOPHAGIA (DIRT-EATING) IN CHILDREN

A Report of Sixty Cases

Joseph E. Gardner, M.D., and Fethi Tevetoğlu, M.D.
Corpus Christi, Texas

WE HAVE not been able to find in the literature a study using x-ray as a routine means of diagnosis of geophagia. Different forms of pica, however, have been studied by this means for many years, and roentgenograms have frequently been of help in the investigation of pica or its complications, in lead poisoning,[2, 3, 10, 11, 13, 16, 18] bezoars,[1, 6] location of foreign bodies,[7, 8, 9, 12] and other conditions.

Pica is a craving for unnatural objects. Geophagia is the eating of dirt.

In 1952, Van der Sar and Waszink[17] used x-ray to show numerous stones in the colon of an obstipated Negro child.

The first report of the use of x-ray in the diagnosis of geophagia was by Clayton and Goodman[4] in 1955. These authors reported four cases of dirt-eating in Negro women, and suggested that x-rays of the abdomen may be helpful in this diagnosis. We are using x-ray examinations routinely in all patients suspected of geophagia.[14, 15]

Since this study began four years ago, sixty cases have been followed. These patients, all under 5 years of age, are proved dirt-eaters and had anemia, achlorhydria, and dirt in the feces. Many of them have been observed for two years or more. Many other cases, which have not been completely studied, are not included in this report.

We do not propose to define or discuss pica other than geophagia. This has been done in a previous report.[15] Those interested in more detailed information on pica are referred to Cooper's excellent monograph.[5]

Theories of etiology, clinical manifestation, treatment, and complications have also been described.[5, 15]

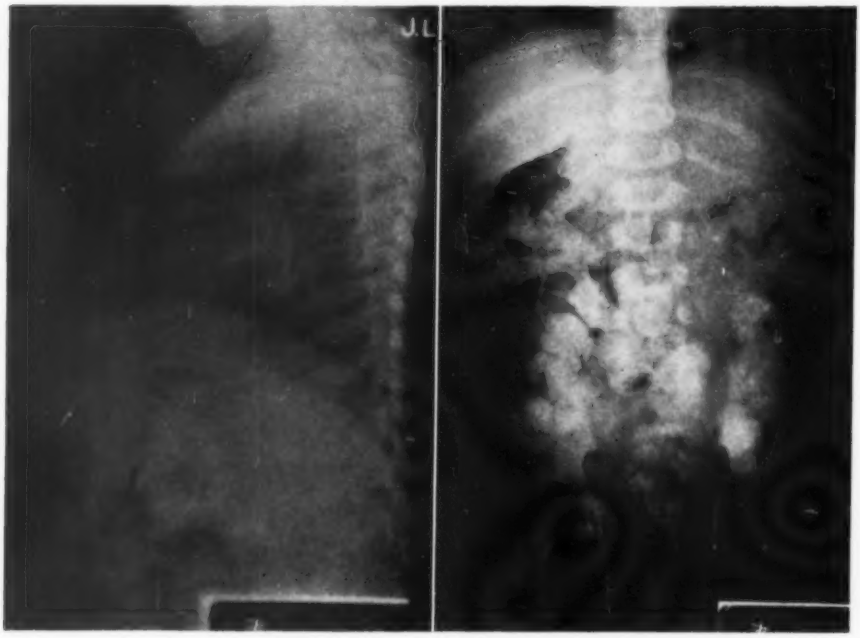
Our discussion of geophagia is limited to that seen in infants and children. It is the purpose of this paper to show the importance of the recognition of geophagia on the roentgenogram.

METHODS AND MATERIALS

Sixty children, ranging from 11½ months to 4½ years of age, from the Driscoll Foundation Children's Hospital are included. There are fifty-three Latin Americans (twenty-nine females and twenty-four males), four Anglo-Americans (two females and two males), and three Negroes (all male). All patients seen in this hospital and outpatient clinic come from low-income families. All are residents of Nueces County, Texas. Thirty-five live in Corpus Christi, twenty-five in nearby rural sections, and all have easy access to earth.

From the Driscoll Foundation Children's Hospital.

X-ray, as a method, was used as a primary as well as a secondary means of diagnosis. The primary group came to the clinic for complaints unrelated to geophagia. These patients had x-ray examinations of the chest, spine, abdomen, pelvis, or hips. The diagnosis of geophagia was made incidentally (Fig. 1). In the secondary group the abdomen was examined by x-ray to confirm the suspicion of geophagia either from history or anemia.



A. *B.*

Fig. 1.—*A*, Lateral chest film of a child showing opaque material in the colon. Geophagia was unsuspected until this radiograph was taken. *B*, Anteroposterior view of abdomen of same patient.

Anteroposterior view of the abdomen was sufficient examination for demonstration of presence of dirt in the colon. In all cases it was important to rule out the ingestion of any medicine or administration of heavy metals such as barium or bismuth. In patients with large amounts of ingested material in the colon, chest films are sufficient for the diagnosis.

The appearance of dirt in the colon was fairly constant and varied only in amount of material present. The dirt appeared dense and amorphous and the size of the individual aggregations of opaque material varied greatly. The density was approximately that of bone cortex. The colon usually contained large amounts of fecal material consistent with the usual history of constipation (Figs. 1-4).

The dirt eaten by the patients contained, grossly, small grains of sand, pieces of metal, roots, or leaves.

Fig. 2.

Fig. 3.

Fig. 4.

Figs. 2, 3, and 4.—Typical appearance of geophagia as seen on films of the abdomen showing the wide variation in amount of opaque material as well as the fairly large foreign bodies as seen in Fig. 1. Note that all these show a large amount of fecal material in the colon, compatible with constipation.

TABLE I. THE RESULTS OF SEMIQUANTITATIVE SPECTROGRAPHIC ANALYSIS FROM FOUR SAMPLES OF SOIL

ELEMENT	APPROXIMATE PER CENT			
	CASE 1	CASE 2	CASE 3	CASE 4
Copper	0.001	0.0009	0.003	0.001
Tin	Not detected	Not detected	0.04	Not detected
Lead	Not detected	Not detected	0.03	0.03
Iron	0.7	1.0	2.0	1.0
Silicon	32.0	33.0	43.0	38.0
Manganese	0.03	0.07	0.03	0.04
Chromium	0.002	0.002	0.004	0.003
Vanadium	Trace	Trace	Trace	Trace
Aluminum	2.0	3.0	3.0	5.0
Magnesium	0.2	0.2	0.3	0.5
Calcium	1.0	4.0	9.0	6.0
Titanium	0.08	0.1	0.08	0.2
Sodium	0.2	0.1	0.2	0.2
Barium	0.03-0.3	0.03-0.3	0.03-0.3	0.03-0.3
Strontium	Trace	Trace	Trace	Trace
Zirconium	0.008	0.02	0.008	0.01

A semiquantitative spectrographic analysis was run on four cases (Table I). Two of these cases failed to show radiographic evidence of geophagia (Table I, Cases 1 and 2). No definite conclusions can be drawn from this analysis, but it should be noted that the calcium content of the soil samples showing on the x-ray is relatively high (Table I, Cases 3 and 4).

The amount of dirt ingested by different patients varied widely. This is the one cause of the wide variation of the pattern of opaque densities in the colon.

Patients admitted to the hospital showed no evidence of dirt in the colon after three to ten days. Those patients treated at home showed dirt in the colon for several weeks, indicating that dirt-eating continued. After the colon has been cleansed, the opacity is no longer visible.

DISCUSSION

We feel that the radiographic recognition of geophagia is of more than academic interest. We have seen one child, a private patient, so severely anemic from dirt-eating that he was unable to walk. He had been treated with numerous vitamins, hematinics which included folic acid, B_{12}, iron, and liver preparations. There was no response. The dirt in the colon was incidentally identified on a chest film. There was a rapid improvement following the cobalt-iron mixture therapy. This response to cobalt-iron was consistently present in all cases.

In our series we found that forty-seven of sixty cases showed opaque material in the colon. The remaining thirteen cases showed dirt in the feces on direct examination. All showed hypochromic, microcytic anemia associated with achlorhydria. Twenty-six of these sixty patients had been seen before dirt-eating began. All had normal hemograms at that time and x-rays of the abdomen or chest were negative for opaque materials. After dirt-eating began, all of these showed evidence of dirt in the colon and a marked anemia as well as achlorhydria.

There were thirteen cases (including Cases 1 and 2, Table I) showing gross dirt in the stools, achlorhydria, and microcytic, hypochromic anemia, in which we were unable to demonstrate

opaque material in the colon radiographically. We are unable to explain this unless the type of dirt in these cases was different or the amount insufficient to show on the x-ray. Several of these were very early dirt-eaters. It may take some time for enough dirt to accumulate to show on the radiograph.

SUMMARY AND CONCLUSIONS

The radiographic picture of geophagia (dirt-eating) is presented in sixty cases. The clinical significance of these findings is discussed. Typical radiographs are shown. The results of semiquantitative spectrographic analysis from four samples of soil are presented.

All patients with an unexplained iron-resistant anemia, or achlorhydria, or whose history would lead one to suspect dirt-eating should have x-rays of the abdomen to determine the presence or absence of dirt in the gastrointestinal tract.

We express our appreciation to Mr. Herbert M. Shilstone, Jr., Director of Shilstone Testing Laboratory, Houston, Texas, for analysis of soil samples, and particularly to Mr. Jessie L. Gill and Robert L. Brown, x-ray technicians, for technical assistance rendered.

REFERENCES

1. Allen, L. G.: Phytobezoar, Am. J. Roentgenol. 39: 67, 1938.
2. Caffey, J.: Clinical and Experimental Lead Poisoning: Some Roentgenologic and Anatomic Changes in the Growing Bones, Radiology 17: 957, 1931.
3. Caffey, J.: Lead Poisoning Associated With Active Rickets: Report of a Case With Absence of Lead Lines in the Skeleton, Am. J. Dis. Child. 55: 798, 1938.
4. Clayton, R. S., and Goodman, P. H.: The Roentgenographic Diagnosis of Geophagia (Dirt-Eating), Am. J. Roentgenol. 73: 203, 1955.
5. Cooper, M.: Pica, Springfield, Ill., 1957, Charles C Thomas.
6. DeBakey, M., and Ochsner, A.: Bezoars and Concretions, Surgery 4: 934, 1938.
7. Delaney, C. J.: Foreign Bodies Swallowed by Children, New York J. Med. 40: 1024, 1940.
8. Gillespie, J. B.: Perforation of Duodenum by Foreign Body: Symptoms Suggesting Disease of the Hip, Am. J. Dis. Child. 80: 600, 1950.
9. Moreau, M. H., and Noguera, O. F.: Ingestion de cuerpos extranos: consideraciones clinico-radiologicas, Semana méd. 1: 1318, 1934.
10. Park, E. A., Jackson, D., and Kajdi, L.: Shadows Produced by Lead in X-ray Pictures of the Growing Skeleton, Am. J. Dis. Child. 41: 485, 1931.
11. Radner, S.: On the Roentgenographic Skeletal Changes in Lead Poisoning in Children, Acta radiol. 25: 719, 1944.
12. Smith, J.: Hair Eating and Pica in Children, Brit. J. Child. Dis. 28: 282, 1931.
13. Stetson, C. A., Jr.: Pica (As Consequence of Iron-Deficiency Anemia); Relationship to Lead Poisoning in Children, J. Maine M. A. 38: 10, 1947.
14. Tevetoğlu, F.: The Treatment of Common Anemias in Infancy and Childhood With a Cobalt-Iron Mixture, Including a Case Report of Iron Deficiency Anemia Due to Geophagia, J. PEDIAT. 49: 46, 1956.
15. Tevetoğlu, F.: Geophagia (Dirt-Eating) as a Cause of Anemia in Children: Report on Sixty Cases, in press.
16. Valquist, B., and Soelde, H.: Lead Poisoning During the Period of Growth, Acta paediat. 31: 180, 1943.
17. Van der Sar, A., and Waszink, H. M.: Pica (Report on a Case), Docum. med. geog. et trop. 4: 29, 1952.
18. Vogt, E. C.: Roentgen Sign of Plumbism: Lead Line in Growing Bone, Am. J. Roentgenol. 24: 550, 1930.

EAR STUDIES IN THE NEWBORN INFANT

Natural Appearance and Incidence of Obscuring by Vernix, Cleansing of Vernix, and Description of Drum and Canal After Cleansing

M. S. McLellan, M.D.,* and C. H. Webb, M.D.
Shreveport, La.

IT IS axiomatic in pediatric circles that the physical examination of a child is not completed until the ears have been visualized. This principle should also apply to the newborn infant. Intrauterine infections attack the fetus, trauma may occur at birth, and only by careful inspection of the external canal and drum can the physician know that abnormal physical signs do not exist. It is a belief among physicians that disease is best diagnosed by first knowing what the part at hand shows in the healthy state; it was their "blind spot" in this sphere of knowledge with regard to the external ear, and their inability to find detailed descriptions of the physical appearance of this structure in the American pediatric literature[1-9] that stimulated the authors to make this study.

Previous sporadic examinations indicated that it was usually impossible to visualize properly the drum and canal because of the c r e a m y material present, but it was considered desirable to support this clinical impression by organized study. The Confederate Memorial Medical Center, Shreveport, Louisiana, having a populous newborn service, was selected for this investigation.

From the Pediatric Service, Confederate Memorial Medical Center.

This work was supported by E. I. McLellan of Sumner, Mississippi.

*Address: 1636 Woodrow, Shreveport, La.

We desired knowledge of what the newborn ears show, and whether they were always obstructed by vernix (Part I); to develop an adequate method of clearing this (Part II); and to determine the appearance of canal and drum after cleansing, if they could not be visualized initially (Part III).

MATERIALS AND METHODS

Patient Material.—The subjects for this study were the term, healthy newborn infants brought to the nursery from the delivery room, less than 24 hours old. All such babies born at Confederate Memorial Medical Center during the period of study were seen if conditions permitted. No selection based on race, sex, exact birth weight, exact age in hours, or past history was made. Most infants were of the Negro race.

General Procedure and Equipment.—All examinations were done by one pediatrician (M. S. M.) to ensure uniformity of results. An ordinary Welch-Allyn otoscope was chosen for examinations; it included an operating head and magnifying lens, and, for most examinations, the large handle with fresh batteries and the "infant" size green nylon speculum, although a few times the small handle and No. 208 speculum were used.

The infants were examined supine. The examiner restrained the child's

head, though assistance, of course, was desirable. The attitude of the baby, whether asleep or awake, quiet or crying, still or struggling, was ignored. In Part I, infants were examined in their bassinets, the nurse tabulating results simultaneously. In Parts II and III, infants were carried to a private room, restrained to a circumcision board, and placed on a standing-height table for ear cleansing and examination. The examiner kept records himself in Parts II and III.

PART I

PHYSICAL APPEARANCE AND INCIDENCE OF OBSCURING BY VERNIX IN THE NATURAL STATE

In Part I, 204 ears in 102 babies were examined. White or grayish-white, semisolid, creamy material obstructed visibility in every ear. We assumed that this material was the same as the vernix caseosa on the skin of the infant. Vernix in several ears was flecked with bright red blood from delivery. One canal showed yellow vernix. The amount varied, at times almost filling the canal, and the drum was never free of it. Hairs, at times missed because of vernix, were seen in 169 ears. Wax was never present. Drum color could never be more than suspected in 88 ears, and was most often grayish. A vague cone of light was suspected in 13 ears. In 24 ears ossicles may have been located but were never well defined. In no instance was a good diagnostic examination with the otoscope possible.

PART II

CLEANSING

Preliminary Efforts.—The soft creamy appearance of vernix gave hope that it could be easily syringed out in the conventional way.[8] When physiological saline was used for syringing, this was not found to be the case. Tap water likewise was of little effect. Saturated solution of sodium bicarbonate was tried but discarded. A commercial baby oil emulsified a small lump of vernix, but when used with the syringe it did not work well. Ethyl ether dissolved particles of vernix promptly. Ether-oil mixtures were tried for syringing but were given up. We substituted the medicine dropper for the glass syringe. Ether instilled and agitated with the dropper was effective and satisfactory.

Ether-Dropper-Swab Method.—At cleansing, ears were first briefly inspected with the otoscope. Then, alternately, the left and right ears were lavaged with ether, allowed to dry and warm up, and swabbed as needed with the cotton-tipped metal applicator. As vernix dissolved, the ether became cloudy and was replaced. The otoscope permitted swabbing under direct vision and observation of progress. It was expedient to use the applicator for removing insoluble flecks of white material assumed to be desquamating epithelium, grayish or black sootlike material assumed to be melanin, flecks of tenaceous vernix, and for blotting residual ether-vernix mixture. We spent ten to twenty minutes and used about 30 ml. of ether for cleansing both ears of an infant; later trials demonstrated that 2 ml. were satisfactory for an ear. During and promptly after cleansing, ears were examined and described.

Results.—A method for removing vernix from the ear was demonstrated. Both ears of 51 infants were consecutively cleansed by the ether-dropper-swab method. Ten per cent of ears

became clean with ether-dropper lavaging alone; in 90 per cent the applicator was also used. Changes in physical signs due to ether lavaging were not detected. No evidence of birth trauma to the ears was found, and trauma from the procedure was limited to rare superficial abrasion by the speculum or applicator. The infants showed little evidence of pain. Responses associated with the caloric test for VIII function were not noted. Cleansing made ear examinations possible.

We have continued to try cleansing by washing only. We have employed other materials. A wetting agent in aqueous solution, recommended for softening wax, affected vernix slightly in 13 ears but did not dissolve or emulsify vernix in the test tube. Oil and ether-oil mixtures used with the dropper and swab cleansed vernix in 15 ears. One milliliter of ether mixed with 1 ml. of oil was sufficient for an ear in some cases. Twenty ears in ten infants were swabbed without lavaging; swabbing, though effective, was potentially more traumatic and cleansed less completely. We have not tried the ring curette on vernix. Vernix was insoluble in glycerin, in acetone, and in ethanol 95 per cent in the test tube. Plain ether was more effective than other materials for cleansing.

PART III

DESCRIPTION OF THE CANAL AND DRUM AFTER CLEANSING

In the first part of this study, inspection of more than 200 ears demonstrated universal obscuring by white creamy material, presumably vernix caseosa; the second part described an effective method of removing this material. The subjects whose ears are described in Part III are the same 51 infants whose ears were cleansed in Part II. An additional 20 ears in 10 infants were cleansed and examined for extra data on canals only in Part III. Drum landmarks sought were those seen in older subjects.

Results.—Table I gives drum data statistically. The most helpful landmark and usually the first identified during cleansing, the one in plainest view, and the one seemingly nearest the examiner was the lateral or short process of the malleus. It lay near the anterior wall and was usually white, occasionally pink, and frequently well defined. Prominence of the short process was probably increased by retraction or medial displacement of the drum, which was usually present. It oriented the drum and pointed out the long process. Description of the drum was impossible until the short process was found.

The long process or manubrium of the malleus was only occasionally well

TABLE I. DESCRIPTION OF THE CLEANSED TYMPANIC MEMBRANES IN FIFTY-ONE TERM INFANTS IN THE FIRST TWENTY-FOUR HOURS OF LIFE

EARS SEEN	PARS TENSA COLOR			PARS FLACCIDA COLOR			CONES OF LIGHT SEEN	SHORT PROCESS OF MALLEUS	TYMPANIC MEMBRANES WELL SEEN
	G	P	R	G	P	R			
102	17	72	13	1	32	69	27	102	102

G = Gray; P = Pink; R = Red.

defined. When visualized, it extended in a straight line from the short process to the umbo. In a few ears the ossicle showed through the membrane, but, usually, it was marked by discrete vessels or increased redness along its axis. This redness contrasted sharply with the tensa anterior and inferior to it. The vessels of the manubrium, as they neared the short process, fanned out over the drum surface above. Retraction, or inward displacement of the drum, was revealed by inward and upward displacement of the manubrium. In extreme retraction, the manubrium was out of sight or barely visible by looking up and under the drum surface overhanging it, and the posterior malleolar fold was thrown into bas-relief. Unless one recalled the anatomy,[10] a prominent posterior malleolar fold could be mistaken for the manubrium. They resembled in contour, horizontal angle, direction, and point of origin at the short process. They differed, of course, in relation to flaccida, tensa, umbo, and canal walls. If the manubrium and posterior malleolar fold could be visualized on the same drum, the differentiation was easy. With less marked retraction of the drum, the manubrium was visible, but foreshortened. Extent of foreshortening, angle with the horizontal, and ease of inspection of the manubrium varied from ear to ear. The horizontal angle was any value between zero and forty-five degrees. The characteristic small circular area at the spatula end of the manubrium was rarely visible. The manubrium in the newborn infant was less helpful as a sign in physical diagnosis than in the adult. The long and short processes and the flaccida lay near the tip of the speculum and were well illuminated by the otoscope.

The flaccida was red or pink with, at times, a purplish cast or, rarely, a grayish cast. It appeared thickened and was opaque. Small vessels frequently crossed it vertically, seeming to disappear near the superior wall. The flaccida lay more in a horizontal plane, whereas the tensa lay more in a vertical. The tensa in horizontal cross section appeared curved, its concavity directed outward. In color it was dusky pink or grayish pink. Frequently, white spokelike markings and, less often, small vessels radiated over its surface from an invisible hub assumed to be the umbo. The tensa was largely dull and opaque. On occasion, however, a small area of translucency was suspected. We wondered whether translucency was influenced by middle ear contents[9] and direction of light rays as well as structure of the drum membrane itself. The cone of light, when present, was small, irregular, and indistinct, and never the glossy cone-shaped light reflex on a translucent tensa seen characteristically in the healthy older infant, child, and adult. These cones were in the usual location. The depth, size, shape, and direction of the canal made examination of the tensa difficult and seemed better adapted for visualization of the flaccida than the tensa with the otoscope. However, diagnostic examination was successfully done in all ears.

An additional 20 ears in 10 infants were cleansed for study of the external auditory canal only. All 20 canals admitted the "infant" speculum. No canal contained visible cerumen. Gray or black material, assumed to be melanin, was removed on cotton tips from all 14 ears of Negro infants; 6

ears of white infants did not show this material at cleansing. Hairs were seen in all 20 ears. In only 2 canals of one infant were hairs long and plentiful enough to obstruct vision. They appeared white in white infants and black, brown, or tan in Negroes; however, hairs were often short, scarce, and fine, making color discrimination difficult and uncertain. The superior wall was visible, and it was shorter than the inferior wall. Its junction with the flaccida, though exposed, was poorly defined. The inferior wall ascended from the drum and external orifice of the canal to a transverse ridge about midway between. This ridge seemed to divide the inferior wall into an outer hairy part and an inner, smooth, glabrous part. This inner portion of the inferior wall was poorly seen because it lay so near and parallel to the line of vision of the examining eye. The superior and inferior walls were wider than the anterior and posterior walls, the latter two walls appearing curved in sagittal cross section; thus a sagittal cross section at the ridge was characteristically oval in shape in 16 ears, with the longer diameter being anteroposterior. In only 4 ears this cross section appeared more round than oval. Depths of 5 canals were determined by sounding with the cotton-tipped metal applicator from the outer surface of the tragus to the tensa and, expressed in centimeters, were as follows: 2.3, 2.2, 2.5, 2.4, and 2.3. The visible portion of canal walls resembled adjacent skin color, being usually pink. Canals often interfered with, but did not prevent, a satisfactory diagnostic examination in any of the ears.

SUMMARY AND CONCLUSION

In Part I, we examined and described the ears of term healthy newborn infants in the first 24 hours of life in the natural state, proving them to be obscured by vernix. In Part II, 102 ears in 51 infants were examined and described after cleansing with ether and an additional 20 ears were cleansed and examined for more data on the canal. Drums were dull, red, thickened, and retracted with poorly defined landmarks. Thus, by adult standards, all drums were abnormal; we postulated that different standards for diagnosis were needed and our findings supported this assumption. The canals were bent, oval in cross section, and contained hairs.

Simpler methods of cleansing and improved instruments for visualization of the newborn ear are needed. These might permit ear examination routinely in the nursery. Continued study is indicated to demonstrate changes which occur in the ears during the neonatal period.

We wish to thank Dr. W. S. Harmon, superintendent of Confederate Memorial Medical Center, for extending his hospitality to us. Drs. J. W. Cotter, M. A. Bodron, and J. D. Jordan, resident pediatricians, showed stimulating interest and offered helpful suggestions. Head Nurses Ashley, Ferguson, and Black, and other staff members, gave assistance in every way possible, along with a congenial, professional, interested attitude that made us feel welcome. Mrs. Corinne McLellan made the manuscript presentable, and saw this study through.

REFERENCES

1. Webb, C. H.: Personal communication.

2. Grulee, C. G., and Bonar, B. E.: The Newborn, Infections of the Middle Ear, *in* Clinical Pediatrics, Vol. III, Edited by R. S. Haynes, New York, 1926, D. Appleton & Company, pp. 369 and 370.
3. Smith, C. A.: The Physical Examination in Neonatal Pediatrics, *in* Nelson's Textbook of Pediatrics, ed. 6, Philadelphia, 1954, W. B. Saunders Co., p. 252.
4. Washburn, A. H.: The Appraisal of Health During Growth From Birth to Adolescence, *in* Brennemann's Practice of Pediatrics, Vol. I, Hagerstown, Md., 1948, W. F. Prior Co., Chap. 8, p. 12.
5. Gordon, H. H.: Diseases of the Newborn Infant, *in* Nelson's Textbook of Pediatrics, ed. 6, Philadelphia, 1954, W. B. Saunders Co., p. 281.
6. Washburn, A. H.: Personal communication.
7. Gordon, H. H.: Personal communication.
8. Burnett, C. H.: Examination of the Ear, *in* Cyclopedia of the Diseases of Children, Vol. IV, Philadelphia, 1890, J. B. Lippincott Co., pp. 7 and 10.
9. Stuart, H. C., and Stevenson, S. S.: Care and Evaluation of Well Children, Neonatal Period, *in* Nelson's Textbook of Pediatrics, ed. 6, Philadelphia, 1954, W. B. Saunders Co., p. 29.
10. Cunningham's Manual of Practical Anatomy, ed. 11, Vol. III, Edited by J. C. Brash, New York, 1948, Oxford University Press, pp. 323-330.

GROWTH AND DEVELOPMENT

I. Relation of Birth Weight in Negro Infants to Sex, Maternal Age, Parity, Prenatal Care, and Socioeconomic Status

E. Perry Crump, M.D., Carrell P. Horton, M.A.
Jitsuichi Masuoka, Ph.D.,* and Donnalda Ryan, B.S.
Nashville, Tenn.

THE existence of mean birth weight differences between various ethnic or racial groups has been well established, but the basic factors which determine these differences remain undefined. To be sure, genetic background plays a strong role, nevertheless such determinants are primarily familial, and less likely racial. In the case of individual family units, where this can be demonstrated readily without particular regard to race, one observes not infrequently 9 or 10 pound infants born consecutively, presumably as a family pattern or trait.

Attempts to explain observed differences in the mean or median birth weight of Negro and white infants range from a simple declaration of biological variations based on race, to other more substantial considerations based on prenatal influences which in turn are dependent upon social, economic, and general environmental factors. Even as recently as 1932, Bivings[1] wrote: "There is a good deal of evidence which would lead one to believe that the pigmented skin of the Negro filters out much of the available ultra-violet light, thus probably playing a part in the production of weakness and lessening birth weight." This statement demonstrates how far opinionated generalization goes.

The following is a partial list of factors, varying in significance and in the directness of their effect, that have been considered by various authors as important determinants of birth weight:

- Racial origin
- Period of gestation
- Type and amount of prenatal care
- Social and economic status
- Maternal age
- Maternal height
- Maternal weight
- Maternal prenatal nutrition
- Maternal education
- Maternal prenatal occupation
- Parity and birth order
- Sex of infant
- Geographic location
- Season

American Negro infants have been reported by numerous authors as having a lighter birth weight on the average than that of white infants, and this phenomenon has been amply demonstrated by gross statistical analysis. The fact that the problem of statistical analysis and interpretation continues to remain a complex one, however, is attested to by the tentative list of influencing factors given in the above paragraph.

Meredith,[2] after bringing together and organizing much of the published data dealing with the average birth weight of North American Negro

From the Department of Pediatrics, George W. Hubbard Hospital of Meharry Medical College.

This investigation was supported by a research grant [No. RG-3761 (CE)] from the National Institutes of Health, Public Health Service.

*Professor of Sociology, Department of Social Sciences, Fisk University.

and white infants, reported that the mean birth weight of the 33,589 Negro infants was 3.28 kilograms (7 pounds 3 ounces) while that for the 109,157 white infants was 3.41 kilograms (7 pounds 8 ounces). On the basis of these findings he concludes: "In general terms, the average North American Negro infant is over one-fourth pound, nearly 4 per cent, lighter at birth than the average North American white infant."

In view of the fact that Meredith[2] has carefully examined the mass of

TABLE I. COMPARATIVE MEAN BIRTH WEIGHTS OF INFANTS OF VARIOUS RACES

RACE	SEX	NUMBER OF CASES	MEAN BIRTH WEIGHT (GRAMS)	AUTHORS	YEAR	CITY	PREMATURE INFANTS EXCLUDED
White							
(Ward)	M & F	1,801	3,402				
(Private)	M & F	955	3,459	Bivings[1]	1932	Atlanta	Yes
Negro	M & F	3,255	3,119				
White	M	608	3,390	Bakwin[3]	1928-	New York	No
	F	609	3,251		1929		
Negro	M	99	3,100	Bakwin[3]	1928-	New York	
	F	88	2,916		1929		
Negro	M	5,466	3,378	Scott et al.[4]	1939-	Washington	Yes
	F	5,226	3,269		1947		
Negro	M	28	3,416	Pasamanick[5]	1946	New Haven	Yes
	F	25	3,199				
White	Mq	71	3,629	Baldwin[6]	1910-	Iowa	
	F	67	3,714		1913		
Negro	M	60	3,408				
	F	70	3,340				
Negro	M	480	3,300	Michelson[7]	1935-	New York	
	F	449	3,100		1936	City	
White	M	150	3,500	Marmour[7]	1935-	New York	
	F	120	3,300		1936	City	
Negro	M & F	1,027	3,185	Meyer[8]	1915	Baltimore	Yes
White	M & F	1,031	3,437				
Negro	M	1,144	3,154	Anderson et al.[9]	1938-	Cincinnati	No
	F	1,153	3,053		1941		
White	M	1,731	3,349				
	F	1,658	3,234				
White	M & F	2,769	3,400*	Dunham et al.[10]	1928-	New Haven	No
Negro	M & F	154	3,090*		1932		
Negro	M	947	3,227	Crump et al.	1951-	Nashville	Yes
	F	874	3,171		1957		
African	M	387	3,189	Shaw[11]	1933	Nairobi	Yes
	F	363	3,104				
Europeans	M	152	3,317	Supplied by Dr. Courlay in London			Yes
	F	139	3,232				
Indians	M	100	2,764				
	F	107	2,888			Nairobi	Yes
Chinese	M	678	3,117	Tso[12]	1921-	Peking	Yes
	F	657	2,980		1929		
Chinese	M	118	3,230	Shan-Yah Gin[13]	1935-	Shanghai &	
	F	110	3,180		1941	Chengtu	Yes

*Median scores. (Taken from Meredith, H. V.: Human Biol. 24: 293, 1952.)

accumulated data, one may accept his conclusion as valid. Nevertheless, in his review of the literature in 1952, comparing birth weights of Negro and white infants, he could find but few reports published after 1940. Five papers were published prior to 1930, and all but one report came from cities of northern or border states. Moreover, little or no socioeconomic evaluation of families was made in these studies, other than a rough breakdown into groups according to some predominant or common factor with social and economic implications.

Table I presents comparative birth weight data for American Negroes and whites, and includes reports published as early as 1915. It is clear from a glance at these reports that, on the average, a quantitative birth weight deficit is characteristic of Negro infants, when compared with whites.

SOCIOECONOMIC STATUS

The importance of the social and economic background has been alluded to by numerous writers in attempts to explain apparent anthropometric differences between Negro and white infants at birth. Not infrequently, however, references to socioeconomic factors have been made either to call attention to the unfavorable position generally occupied by the American Negro, or to suggest that, according to the criteria employed, the samples of whites and Negroes are comparable with respect to socioeconomic status. Thus far, to the best of our knowledge, papers appearing in the medical literature generally have not reflected a thorough study of the socioeconomic background or level of living of families of these infants. The relationship of this crucial factor to the growth and development of Negro infants, therefore, has not been clearly delineated. The following excerpts are representative of the limited consideration given this factor:

> Of the colored births 81.9 per cent occurred in families with an annual income of less than $650 in comparison with 39.6 per cent of the white births. The proportion of colored mothers employed away from home during and after pregnancy is high. The economic status of the Negro population in the United States is, on the whole, much lower than that of the white.[3]

> Infants born at Bellevue Hospital come almost exclusively from poor homes, delivery and hospitalization being free, except in rare instances. Infants born at the Fifth Avenue Hospital, on the other hand, come from homes of moderate income, the parents being able to pay about $75 for the cost of delivery.[15]

> Economically about 50 per cent of these infants could be classified as indigent. The remaining group consisted of pay patients, many of whom were delivered by private physicians.[4]

> There is a marked difference between the birth weights of the Negroes of a corresponding economic level in the white race, with only slight differences between private and ward white patients. In the Emory University Hospital, practically all the patients come from the best strata of society and furnish a group for comparison with a lower economic level as seen in Grady Hospital.[1]

> Because of the distribution of the white and Negro population in a group of approximately the same economic status, and because Cincinnati does not provide facilities for home deliveries, this appeared to be a satisfactory sample for study.[9]

> The infants (Negro and white) were unselected except in terms of socioeconomic status, all the mothers being admitted to the ward service of the hospital. All infants under the care of private physicians were eliminated from the study.[16]

> For evaluation of economic status patients were grouped according to hospital pay status into the following groups: (1) private patients delivered by members of the obstetric staff, (2) patients in the ward service who were paying for hospitalization, and (3) free or indigent patients.[17]

Many other factors besides ancestry are known to be associated with gain in weight.

Of these many factors, only two, both of which permit a rather crude estimate of the socioeconomic status of the child's family were considered in the present study. These two factors are: (1) receipt of assistance by the child's family, such assistance coming from either public or private sources, and (2) crowding in the child's home.[18]

The present study, therefore, is undertaken in part to meet this need. It seeks to ascertain the significance of a thoroughgoing evaluation of the relation of the birth weight and subsequent growth and development of Negro infants to such influences as living standards, age, parity, education, nutrition, postnatal weight, prenatal care, occupation of mother, and other potential determinants. Only sex, parity, maternal age, prenatal care and socioeconomic status will be considered in this report.

METHODS AND MATERIALS

In this study of 2,081 cases, data are drawn from three separate sources: namely, (1) Group I, the major continuing study; (2) Group II, the pilot study which preceded the major study, and (3) Group III, a one-year study of all newborn infants in Hubbard Hospital, exclusive of those babies in Groups I and II.

Group I.—This group includes data from 400 newborn infants and their parents. These infants represent single births except for seven sets of twins, and were born between December, 1953, and August, 1955. Data on each infant include the following items of information, not all of which are under consideration at this time:

1. Physical measurements of the infant, including weight, height, head circumference, chest circumference.
2. Bone-age x-ray study of the infant.
3. Reflex maturity score of the infant.
4. Mother's medical-social history.
5. Pre- and post-natal nutritional history of the mother.
6. Socioeconomic index of the family.

Group II.—Group II includes records of 631 infants and their parents. These infants were single births, except for 15 twins, not necessarily paired, and were born between July 30, 1951, and Jan. 30, 1953. Socioeconomic indexes are available for only approximately one-third of the cases. Some aspects of the mother's medical-social history are included on all the records, but other aspects found in Group I are not available for Group II (e.g., parents' height and weight, total number of visits for prenatal care, father's age).

Group III.—The data for Group III were drawn from a survey of all infants born in Hubbard Hospital between Feb. 10, 1955, and Feb. 29, 1956, who were not included in the Main Study project (Group I). This group contains data on 1,050 infants, 23 of whom were twins, not all paired. Only those aspects of the mother's medical-social history available from her hospital record are included. The socioeconomic index used for this group represents a modification of the technique adapted for use with Groups I and II.

It will be noted that in the total of 2,081 infants included in this study, 52 (2.5 per cent) were classified as multiple births (twins).

Selection of Participants.—Only those infants whose mothers reside in the city of Nashville and who were delivered at Hubbard Hospital were studied. The participating mothers in

Groups I and II were contacted prior to delivery in most instances. It was during this initial interview that relevant data on nutritional intake and socioeconomic status were obtained by a nutritionist and a medical social worker. In the case of mothers on the Major Study (Group I), commitments were solicited in order to have them agree to participate in a project designed to follow the infants' growth progress at regular intervals over a five-year period. These expectant mothers were contacted in the Obstetrical Clinic at Hubbard Hospital, and elsewhere in the case of private patients.

No contact prior to delivery was made for mothers in Group III. All information and measurements were obtained after delivery while mother and child remained in the hospital.

Physical Measurements of the Infant.—Measurements of the infants' height, weight, head and chest circumferences were made by selected members of the pediatric staff of Hubbard Hospital. Accuracy of results was verified periodically and uniformity in technique and procedure was routinely followed. Each infant was measured between 12 and 72 hours after birth, and no infant seriously handicapped by birth injury, congenital anomalies, or any other cause was included.

Mother's Medical-Social History.—Data pertaining to the mother's medical and social background were collected by the medical social worker, partly from interviews with the mother upon delivery, and partly from the mother's hospital record. In general, information pertaining to the father was obtained from the mother.

Socioeconomic Index.—Since the relationship between socioeconomic status of the mother and the infant's growth and development is the principal area of investigation in this study, it is deemed necessary to explain the nature of the index in some detail. Two comparable, but slightly different, indexes are used: (1) a more detailed index for Groups I and II, and (2) a briefer index for Group III.

The more detailed index involves the assignment of scores to the following items of information:

1. Occupation of father (or mother, where necessary).
2. Education of father.
3. Education of mother.
4. Chapin living room scale.[19]
5. Modified Sewell scale.[20]
6. Income of father (or mother, where necessary).
7. Contract monthly rent (or 1 per cent of house value if home is owned).
8. Purchase price of automobile.

Information on these items was obtained by the medical social worker, especially trained for this purpose. Information on parent's occupation and education, rent, and purchase price of car was obtained through interviews, and on the remaining items, living room scale and Sewell scale, by observations in the home. (See appended socioeconomic scoring sheets.) The final index consists of a scale which has a range of 0 to 72, allotting 9 points as a maximum value for each item in the index. High scores indicate high socioeconomic status.*

*When one or more of the eight scalable items of information could not be obtained, or was unknown, that item was given the average point value of all of the known items. For example, if contract monthly rent was unknown (or the informant refused to give the information), and the family had a total score of 42 on the 7 other items in the index, "rent" was given a score of 6 (42 divided by 7), making a total score of 48. This practice was followed uniformly in order to have some rating on each of the 8 index items.

The socioeconomic index for Group III consists of only 4 items. This index was tested for comparability with the more comprehensive index, and was found to be a sufficiently reliable measurement, within broad limits. No visits to the home were necessary to obtain this rating. The items included are:

1. Occupation of father (or mother, where necessary).
2. Education of father.
3. Education of mother.
4. Marital status.

A maximum of 9 points was assigned to each of the four major items, and the total score was doubled to obtain the final score. Score assignment to marital status, which is the only new item in this index, is more flexible than in the case of any other item. The score of 0 was given to unmarried mothers. The score for widowed, separated, and divorced mothers ranged from 1 to 3, depending on the average of the other items, and the score for married mothers was similarly computed within the range of 4 to 8. In some isolated instances it was possible for the score for widows, divorced, and separated mothers to exceed 3, where it was apparent that the break in the family occurred after conception and/or delivery of the child. This flexible method of scoring was designed to prevent over- or underscoring marital status.

When a final socioeconomic score is obtained, a family is then classified into one of the 4 broad socioeconomic groups previously found to be the most discriminating dividing points for this particular population. The limits of these groups are:

Group I:	0-14	Low
Group II:	15-29	↓
Group III:	30-49	
Group IV:	50 and over	High

RESULTS

Sex of Infant.—The presence of sex difference in the mean birth weight of infants is well known, and this is true regardless of race. All studies of birth weight show that male infants, as a group, are heavier than females.

Table II reveals the mean birth weights by sex of 1,821* of the infants included in this study. The data show that males, on the average, are 99 grams heavier than females, they show a greater variability in birth weight, and predominate numerically.

The Maternal Influence.—All determinants of birth weight act principally through the mother, from conception to delivery, for she provides 100 per cent prenatal environmental control, and at least 50 per cent in genetic background. Therefore, it is reasonable to assume that such factors as maternal age, prenatal care, parity, and socioeconomic status should show some degree of correlation with the weight of the infant at birth.

*Premature infants excluded.

TABLE II

SEX	NO. OF CASES	MEAN BIRTH WEIGHT			STANDARD DEVIATION
		GRAMS	POUNDS	OUNCES	
Male	947	3,227	7	1	±409
Female	874	3,128	6	14	±386
Total	1,821	3,179	7	--	±401

Age of Mother.—A previous study here[21] showed that maternal age at delivery bore no relationship to the incidence of prematurity. In the present study of the 2,045 infants under consideration, the proportion of premature infants is fairly evenly distributed among mothers of all age groups (Fig. 1).*

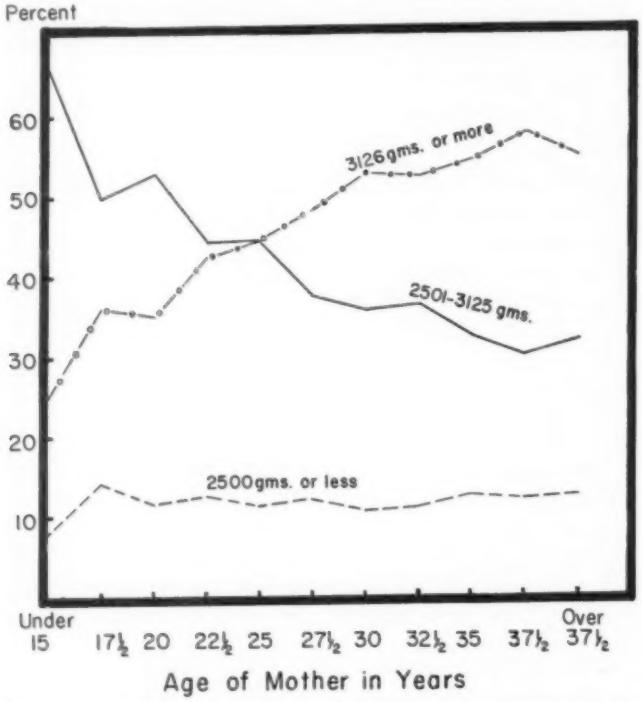


Fig. 1.—Specific birth weights of 2,045 infants by age of mother at delivery, in percentages.

The maternal age at delivery, however, shows a positive relation with birth weight of the infant when the two weight categories, 2,501 to 3,125 grams, and 3,126 grams and over, are considered (Fig. 1). The middle group (2,501 to 3,125 grams) accounts for more than 50 per cent of the infants born to mothers under 20 years of age. With increase in maternal age, however, there is a continuing decline in the frequency with which these infants are born. Conversely, there is an increase in the percentage of infants born in the higher weight category 3,126 grams and over). Thus, from these observations it is possible to state that although no relationship seems to exist between maternal age and the prevalence of the smallest infants, there is a general tendency for younger mothers to have lighter babies, and for older mothers to have heavier infants.

*In the majority of the charts in which birth weights are presented in terms of percentages, the weights are combined into three weight groups: 2,500 grams or less, 2,501 to 3,125 grams, and 3,126 grams or more. The first group represents infants who are considered premature in terms of weight. The second and third groups were delineated by dividing the groups at a point as close to 7 pounds as was possible, in view of the way in which birth weight figures are coded in this study. The dividing point of 3,125 grams is equal to approximately 6 pounds 14⅛ ounces.

The following questions might naturally arise in connection with these observations: (1) Is there a greater proportion of multiparous mothers in the older age group? (2) Are the older mothers larger, particularly heavier? (3) Do the older mothers represent a superior group socially and economically? Data from 1,497 cases in the present study reveal a significant and direct relationship ($r = 0.56$) between the mother's age and her parity.

The correlation between age of mother at delivery and her weight 48 to 72 hours after delivery is found to be 0.2863 for 1,367 cases. Therefore, we may conclude that there is some slight association between age of mother and her weight. Table III reveals the age distribution of the mothers included in this study.

Michelson[7] has pointed out that the age distribution of the mothers whose children are studied may indirectly influence the average birth weight computed in a given survey, inasmuch as the ratio of first-born children is higher and the proportion of infants of smaller birth weights is greater among younger mothers.

Cawley[23] concluded that at birth maternal age has virtually no influence on weight and length of the infant. It is of interest to note that, with respect to birth weight, the same conclusion was reached tentatively from data in the present study, until the infants were grouped into three categories (2,500 grams and less; 2501 to 3,125 grams; 3,126 grams and above). As previously mentioned, younger mothers gave birth to a significantly larger number of infants in the middle group than did older women.

Peckham[24] pointed out that the young woman at term gives birth to an infant smaller in weight but equal in length to that of the more mature individual; however, he found no correlation between maternal age and the true incidence of prematurity.

Tandy[25] from a national survey of 249,706 Negro and 1,844,446 white mothers found that 23 per cent of the Negro mothers were under 20 years of age, compared with 11 per cent of white mothers. He further found that 55 per cent of Negro mothers were under 25 years, while only 41 per cent of white mothers fell into this category. From the age distribution of Negro mothers included in the present study, it will be seen that 21.7 per cent are under 20 years of age, and 55.3 per cent under 25 years of age.

In summary then, it may be stated that data from the present study show a direct and significant relationship between young mothers and small babies. The higher incidence of younger mothers among Negroes (23 per cent under 20 years of age as compared with 11 per cent for whites), combined with the apparent influence of maternal age on birth weight, would suggest that the age of the Negro mother is a contributing factor in the relatively smaller birth weight of the Negro infant. It will be noted that the data indicate no relationship between maternal age and prematurity.

Parity.—Of the total of 1,972 mothers, for whom data on parity are available, the mean parity was 2. It is interesting to note that nearly one-half (47.0 per cent) were para 1 or less at the time of delivery (Fig. 2), and nearly two-thirds were para 3 or less. While more than one-fourth (26.8 per cent) were para 0, only 4.1 per cent of the mothers were para 7 or more (Table IV).

TABLE III. AGE OF MOTHERS AT DELIVERY AND BIRTH WEIGHT OF INFANTS (2,045 CASES)

	UNDER 15 YEARS	15-17½	17½-20	20-22½	22½-25	25-27½	27½-30	30-32½	32½-35	35-37½	37½ YR. AND OVER	TOTAL
Number	12	128	305	366	321	262	218	153	110	83	87	2,045
Per Cent	0.6	6.2	14.9	17.9	15.7	12.8	10.7	7.5	5.4	4.0	4.2	100.0
Mean Birth Weight (Grams)	2,938	2,958	2,982	3,040	3,040	3,052	3,124	3,109	3,159	3,186	3,014	3,058

TABLE IV. PARITY, MEAN AND MEDIAN BIRTH WEIGHTS OF INFANTS BY PARITY (1,972 CASES)

	0	1	2	3	4	5	6	7 AND OVER	TOTAL
Number	528	401	337	264	182	112	67	81	1,972
Per Cent	26.8	20.3	17.1	13.4	9.2	5.7	3.4	4.1	100.0
Mean Birth Weight (Kg.) of Infants	2.98	3.04	3.06	3.06	3.13	3.13	3.16	3.20	3.05
Median Birth Weight (Kg.) of Infants	2.99	3.06	3.06	3.10	3.16	3.19	3.17	3.20	3.14

TABLE V. MEAN BIRTH WEIGHT AND PARITY BY SOCIOECONOMIC GROUP*

SOCIOECONOMIC GROUP	NO. OF CASES	MEAN PARITY	MEAN BIRTH WEIGHT (GRAMS)	MEDIAN BIRTH WEIGHT (GRAMS)
I (Low)	382	3 (2.61)	2,960	2,994
II	657	2 (2.33)	3,038	3,058
III	396	2 (1.88)	3,106	3,116
IV (High)	137	1 (1.30)	3,193	3,236
Total	1,572		3,050	3,071

*Prematures included.

The apparent relationship between parity, socioeconomic status, and birth weight is shown in Table V.

It may be noted from Table V that there is a positive association between socioeconomic status and birth weight, and that while it might be anticipated that the larger infants (in the higher socioeconomic groups) would be associated with higher parity, the converse is found in the present study. Despite the low mean parity of socioeconomic Group IV, its babies were heavier than those in Group I by 227 grams.

It is apparently significant that more than 50 per cent of mothers in the highest socioeconomic group were para 0 and 1, while this was not true of any other group. Moreover, none of the mothers in socioeconomic Group IV were more than para 6,* while 11.2 per cent of the mothers in Group I were para 6 or more.

Parity showed no particular influence upon frequency of premature birth (Fig. 2). The mean incidence of prematurity in the group studied was approximately 12 per cent, and this corresponds closely to the figure found in a previous study in this hospital (11.3 per cent[21]).

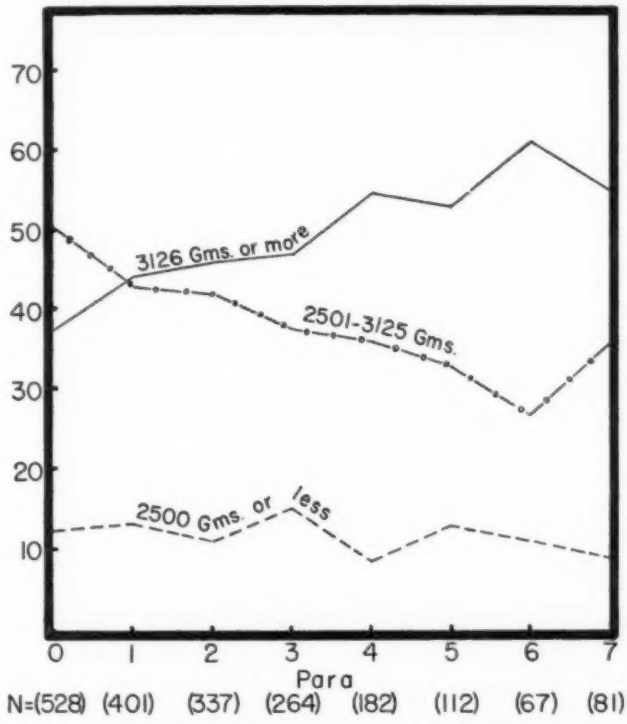


Fig. 2.—Specific birth weights by parity, in percentages (1,972 cases).

It may be noted in Fig. 2 that if the middle (2,501 to 3,125 grams) and highest (3,126 grams and above)

*Seven-tenths per cent were para 6 in socioeconomic Group IV.

groups are combined, one cancels out the other, and thus the existing relationship between parity and birth weight becomes hidden. Since the proportion of premature infants is fairly constant for each degree of parity, so also is the proportion of full-term infants.

Fig. 3, however, reveals a direct and positive association between parity and the infants' birth weight, when data from all babies (including prematures) are combined.

In summary, it may be stated that, as in the case of maternal age, parity exerts a determining influence on birth weight. In general, the greater the parity, the heavier the infant at birth. This must be qualified, however, by the relationship between socioeconomic group, parity, and birth weight. Although the higher socioeconomic groups have a lower mean parity, the mean birth weights still show a consistent increase from the lowest to the highest socioeconomic group. This

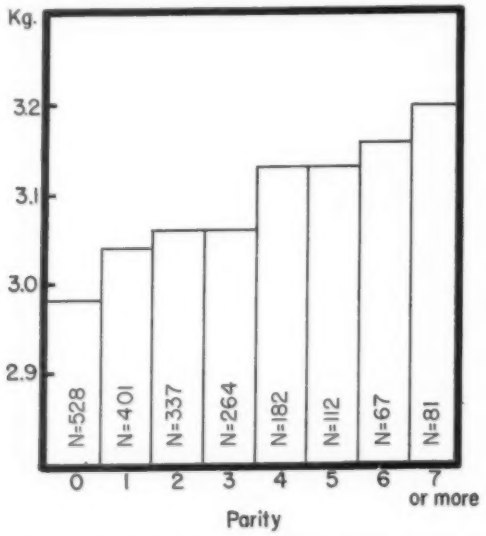


Fig. 3.—Mean birth weights of 1,972 infants, by parity (prematures included).

Taff[22] found that when all races were considered in Hawaii except for the first and the eighth child, parity appeared to make no great difference in the percentage of immature births among the 14,182 single live births reported in 1951.

Peckham[24] found that small infants were born to primiparas more frequently than to any other parous group.

would suggest that, in this study at least, the determining influence of socioeconomic status on birth weight is greater than the influence of parity.

Prenatal Care.—A total of 2,009 cases were available for study to determine the influence of type of prenatal care on the birth weight of the infant, and it was found that prenatal care and birth weight are significantly related (Fig. 4).

When full-term and premature babies are considered, the mean birth weights of both male and female infants are highest for those mothers who had private care, and lowest for those who had no prenatal care. The percentage of premature infants was correspondingly highest for those mothers with no prenatal care (19.8 per cent), and lowest for mothers with private prenatal supervision (7.6 per cent). Those mothers who had private prenatal care generally sought medical supervision earlier in their pregnancy, and made more visits than did the mothers who made use of clinic services.

No relationship could be shown between birth weight and trimester in which prenatal care was begun, nor did the number of visits for such care seem to be related to weight at birth.

Type of prenatal care seems to have a positive influence on duration of gestation in the 1,664 cases studied (Fig. 5).

Significant differences exist between private patients and those who received no care, on the one hand, and between clinic patients and those without prenatal care, on the other.

When considering socioeconomic score by type of prenatal care, the average socioeconomic score was found to be 45 for private cases, 22 for clinical cases, and 21 for those cases with no prenatal care (Fig. 6).

In terms of the grouping of socioeconomic scores used here, the average for private cases falls in socioeconomic Group III, while the average for both clinical and no prenatal care cases falls in Group II. A Chi-square test for independence of socioeconomic score and type of prenatal care (excluding those cases with no prenatal care) proves to be highly significant, indicating that there is some association between the two attributes. The contingency coefficient for those two attributes is 0.50.

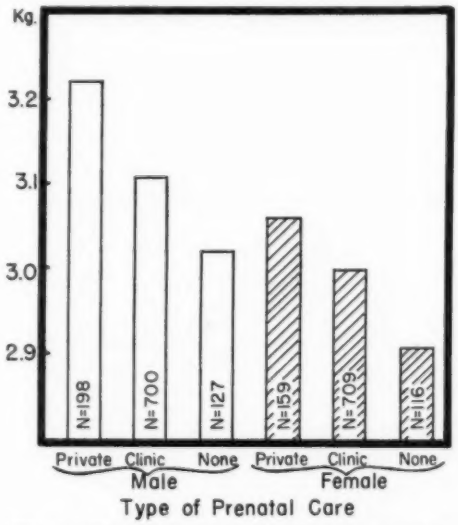


Fig. 4.—Mean birth weight by type of prenatal care.

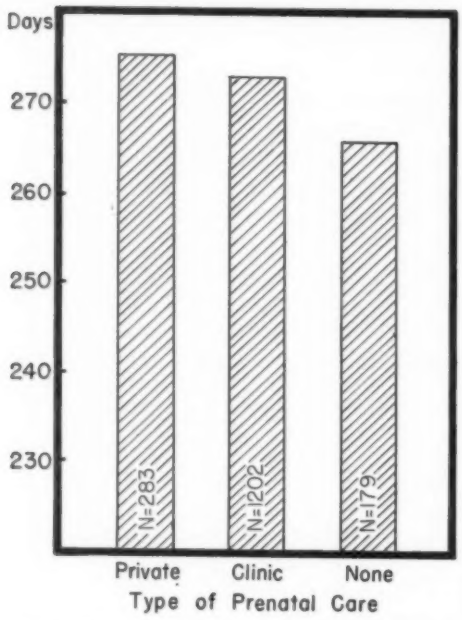


Fig. 5.—Mean gestation period by type of prenatal care (1,664 cases).

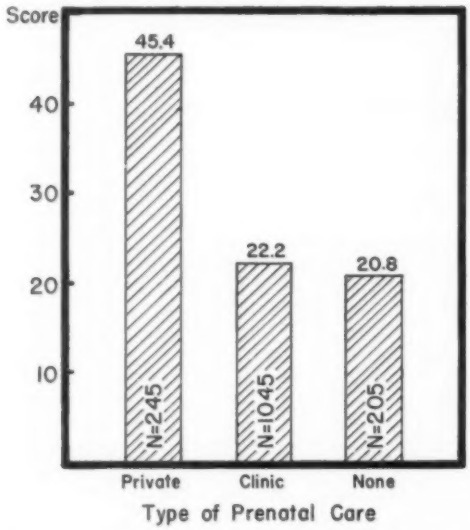


Fig. 6.—Mean socioeconomic score by type of prenatal care (1,495) cases).

TABLE VI

	PRIVATE PRENATAL CARE ONLY	PRIVATE DELIVERY ONLY	PRIVATE PRENATAL CARE AND DELIVERY	ALL CASES
a. Mean Birth Weight (All babies)				
Male	3,076	3,216	3,230	3,116
(No. of cases)	(21)	(9)	(177)	(1,053)
Female	2,699	2,938	3,078	2,995
(No. of cases)	(9)	(3)	(150)	(1,016)
b. Mean Birth Weight (Excluding premature infants)				
Male	3,237	3,216	3,308	3,227
Female	3,117	3,250	3,148	3,128
c. Mean Age of Mother at Delivery	26.5	27.8	26.8	25.2

Examination of the cases which are considered private (according to prenatal care, delivery, or both) provides some interesting findings. Comparative means for private cases and all cases (with private cases included in the total) are shown in Table VI for birth weight and age of mother.

It should be noted that there were very few cases included in the "Private Prenatal Care Only" and "Private Delivery Only" groups. Further, it is noted that in the largest number of private cases (Private Prenatal Care and Delivery), the mean birth weights for both male and female infants are higher than the means for all cases. Mothers who received private prenatal care were, on the average, more than one year older at delivery than all mothers. When comparing "private" cases with "clinic" and "no prenatal care" cases, average birth weight is highest for "private" cases and lowest in the case of those mothers with no prenatal care. Considering the later mean age of mothers with private prenatal care, and the association between type of prenatal care and socioeconomic status, these findings support those observed earlier with regard to age of mother at delivery and birth weight, and also those that are disclosed later in the paper with regard to the relationship between socioeconomic status and birth weight.

Socioeconomic Status.—A total of 1,572 cases comprise the sample for study of the relationship of socioeconomic status to birth weight of Negro infants. The striking influence of this factor on the incidence of prematurity is observed when the complete sociometric scale is used (Fig. 7). The mean percentage incidence of prematurity, for those infants on whom socioeconomic data are available, is 13.3. Fig. 7 reveals that prematurity is almost double this value in the lowest socioeconomic bracket, while it is less than one-half as frequent in the highest.

When the cases were classified into the four major socioeconomic groups (Fig. 8) and arranged according to birth weight categories, it was shown that with increase in standard of living there was an associated increase in the incidence of heaviest babies from 37.4 per cent (socioeconomic Group I) to 59.1 per cent (socioeconomic Group IV). Concomitantly, the frequency of

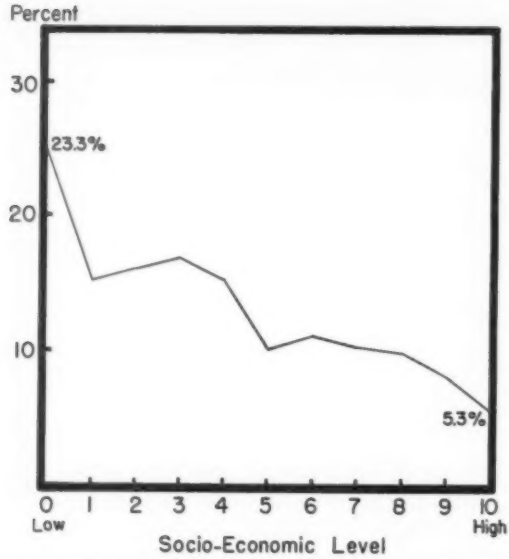


Fig. 7.—Percentage incidence of prematurity by socioeconomic level.

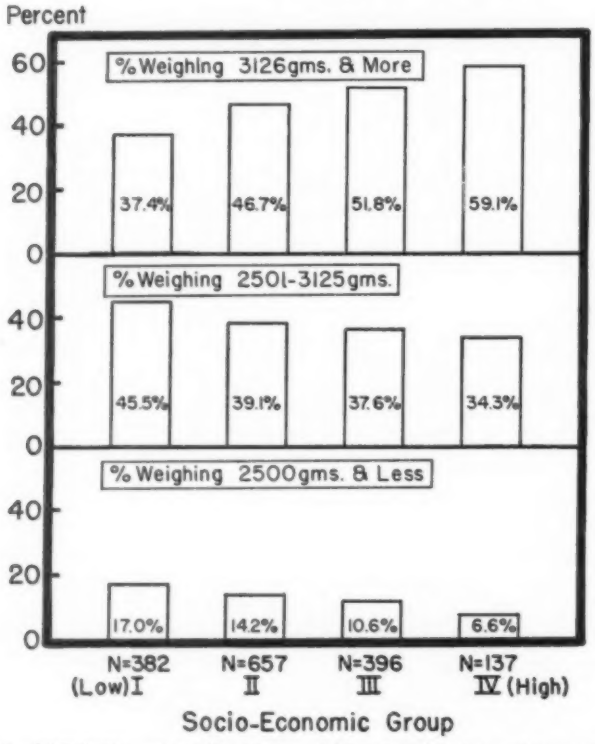


Fig. 8.—Distribution of specific birth weight categories, by socioeconomic group.

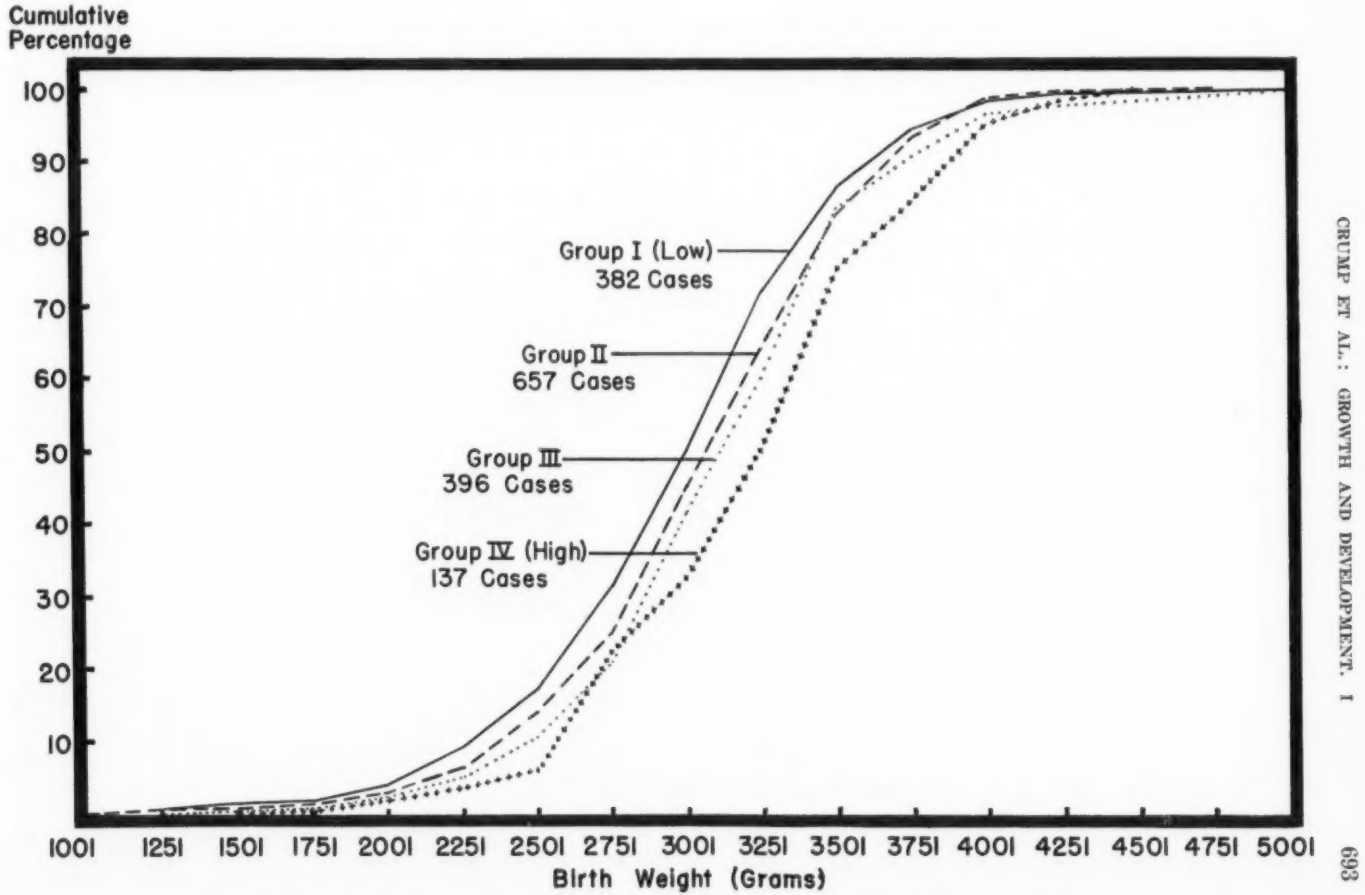


Fig. 9.—Cumulative percentage distribution of birth weights of 1,572 infants, by socioeconomic group.

birth of infants in the 2,501 to 3,125 gram category decreased from 45.5 to 34.3 per cent.

The cumulative percentage distribution of birth weight of infants in each of the four socioeconomic groups is shown in Fig. 9. From this chart it is evident that there is a consistent association between socioeconomic status and birth weight.

The association of socioeconomic status and birth weight has been found to be statistically significant for this study through the technique of covariance analysis. A direct positive association was found both in unadjusted analysis, and with adjustments made for age of mother and/or parity. Premature infants were included in the covariance analysis.

Scott and his associates[4] have shown the relationship of the mean annual per capita income to birth weight of Negro infants in the District of Columbia. They observed that throughout the period of their study (1939 to 1947), the per capita income in the District of Columbia was consistently higher than the general income for the country at large. Because Negro families in Washington shared in this economic advantage, Scott attributed the relatively high birth weights of Negro infants in his study to the more favorable economic condition prevailing during the period of observation.

In summary, the relationship between socioeconomic group and birth weight for this study is such that an increase in socioeconomic level is associated, on the average, with an increase in birth weight. This relationship exists even though the average parity of the highest socioeconomic group is lower than that of any of the other three groups, and parity is one of the factors found to affect the birth weight of infants. The conclusion that these factors have a positive influence on birth weight is further supported by (1) the association between type of prenatal care and birth weight, where the contingency correlation between type of prenatal care and socioeconomic group is 0.50; and (2) the fact that older mothers tend to have heavier babies, and mothers with private prenatal care (generally in one of the two high socioeconomic groups) average one year older at delivery than do all mothers.

SUMMARY AND CONCLUSIONS

It is established that Negro infants are smaller at birth than white babies. It has not been shown, however, that this is exclusively a racial characteristic. There is considerable evidence to show that the Negro, for the most part, is economically an underprivileged group, when compared with whites. Data in the present study tend to show that there is a direct relationship between small babies at birth and certain conditions more common to the Negro mother. (1) It is shown, for example, that she is younger than the average white mother at conception, and the direct influence of youthfulness in reducing birth weight is demonstrated. (2) A similar relationship is demonstrated statistically between birth weight and prenatal supervision and care. (3) The results also indicate a direct relationship between socioeconomic status of the Negro mothers and the average birth weight of infants within each socioeconomic group. (4) Finally, it is suggested that when

Appendix A
Scale for Socioeconomic Status
Groups I and II

Score	Longest occupation of father*	Education of mother	Education of father	Average annual earnings of father*	Shelter rent at interview	Purchase price of car	Revised form of Chapin's scale	Modified Sewell's scale
9	Professional and semiprofessional	College 4	College 4	$4,500 and over	$90 and over	$1,350 and over	100 and over	110 and over
8	Proprietors, managers and officials	College 3	College 3	$3,500-4,499	$80-89	$1,200-1,349	90-99	100-109
7	Clerical	College 2	College 2	$2,750-3,499	$60-79	$1,050-1,199	80-89	95-99
6	Skilled	College 1	College 1	$2,250-2,749	$50-59	$ 900-1,049	70-79	90-94
5	Semiskilled	Grade 12	Grade 12	$2,000-2,249	$40-49	$ 750-899	60-69	85-89
4	Protective service worker	Grade 11	Grade 11	$1,750-1,999	$35-39	$ 600-749	50-59	80-84
3	Service workers (exclusive of domestic and protective)	Grade 10	Grade 10	$1,500-1,749	$30-34	$ 450-599	40-49	75-79
2	Domestice service workers	Grade 9	Grade 9	$1,250-1,499	$25-29	$ 300-499	30-39	70-74
1	Farm laborer	Grade 8	Grade 8	$1,000-1,249	$20-24	$ 150-299	15-29	65-69
0	Unskilled laborer	Less than 8th Grade	Less than 8th Grade	Less than $1,000	Under $20	Less than $ 150	Under 15	Under 65

*In case of illegitimacy, use mother

APPENDIX B
SHORT-FORM SOCIOECONOMIC INDEX
GROUP III

SCORE	OCCUPATION OF FATHER*	OCCUPATION OF MOTHER	EDUCATION OF MOTHER	EDUCATION OF FATHER	MARITAL STATUS	
9	Meharry student; professional, semiprof.	Prof., semiprof.	College 4	College 4		
8	Proprietor, manager, official; college student	Prop., mgr., official	College 3	College 3	Give average of known values for "Married,"	
7	Clerical	Clerical	College 2	College 2	but no	
6	Skilled	Skilled	College 1	College 1	less than	
5	Semiskilled	Semiskilled	High school 4	High school 4	4, and	*Multiply total score obtained by 2*
4	Protective service worker; high school student	Protective service worker	High school 3	High school 3	no more than 8	
3	Service (except domestic and protective)	Service (except dom. and prot.)	High school 2	High school 2	Divorce, desertion, separation, widow†	
2	Domestic service	Domestic service	High school 1	High school 1	(Use average range of	
1	Farm laborer	Farm laborer	Grade 8	Grade 8	1-3)	
0	Unskilled labor	Unskilled labor	Less than 8th grade	Less than 8th grade	Single	

*Use mother's occupation if father's is unknown.
†If in upper bracket on other characteristics, consider as married.

these various determining factors converge on the Negro woman, a summation effect is manifested by the smaller infant which she produces.

It is apparent from the present study that the range of differences in birth weight existing among Negro infants is similar to that shown when Negro and white infants are compared, and that the data presented tend to explain these differences on the basis of influences unrelated to racial origin.

We wish to express sincere appreciation to Dr. Bernard G. Greenberg for his many helpful suggestions in connection with the statistical aspect of this study.

REFERENCES

1. Bivings, Lee: Racial, Geographic, Annual and Seasonal Variations in Birth Weights, Am. J. Obst. & Gynec. **27**: 725, 1934.
2. Meredith, Howard V.: North American Negro Infants: Size at Birth and Growth During the First Postnatal Year, Human Biol. **24**: 290, 1952.
3. Bakwin, Harry: The Negro Infant, Human Biol. **4**: 1, 1932.
4. Scott, R. B., Jenkins, M. E., and Crawford, R. P.: Growth and Development of Negro Infants, I. Analysis of Birth Weights of 11,818 Newly Born Infants, Pediatrics **6**: 425, 1950.
5. Pasamanick, Benjamin: A Comparative Study of the Behavioral Development of Negro Infants, J. Genet. Psychol. **69**: 3, 1946.
6. Baldwin, B. T.: The Physical Growth of Children From Birth to Maturity, University of Iowa Studies in Child Welfare, Vol. 1, 1921.
7. Michelson, Nicholas: Studies in the Physical Development of Negroes, II. Weight, Am. J. Phys. Anthropol. **1**: 289, 1943.
8. Meyer, Arthur: Contrib. Embryol. **2**: 57, 1915.
9. Anderson, Nina A., Brown, Estelle W., and Lyon, R. A.: Causes of Prematurity, Am. J. Dis. Child. **27**: 523, 1943.
10. Dunham, E. C., Jenss, R. M., and Christie, A. U.: A Consideration of Race and Sex in Relation to Growth and Development of Infants, J. PEDIAT. **14**: 156, 1939.

11. Shaw, Michael: The Birth-Weight of Africans, East African M. J. **10**: 32, 1933.
12. Tso, Earnest: Birth Weight and Growth of Chinese Infants During the First Year, Chinese J. Physiol. **4**: 31, 1930.
13. Shan-Yah Gin: Physical Growth of Chinese Infants, J. PEDIAT. **48**: 275, 1948.
14. Brenton, Helen: Climate and Race as Factors Influencing the Weight of the Newborn, Am. J. Phys. Anthropol. **5**: 237, 1922.
15. Bakwin, Harry, and Bakwin, Ruth M.: External Dimensions of the New-born, Am. J. Dis. Child. **48**: 1234, 1934.
16. Christie, Amos: Prevalence and Distribution of Ossification Centers in the Newborn Infant, Am. J. Dis. Child. **77**: 355, 1949.
17. Kessler, Althea: Growth and Development of Negro Infants. II. Relation of Birth Weight, Body Length and Epiphysial Maturation to Economic Status, Am. J. Dis. Child. **80**: 370, 1950.
18. Jenss, Rachel M.: Gain in Weight and Its Association With Ancestry and Economic Status, Human Biol. **12**: 532, 1940.
19. Chapin, F. Stuart: The Measurement of Social Status, Minneapolis, 1933, The University of Minnesota Press. Reprinted with revisions by Pauline V. Young: Scientific Social Surveys and Research, New York, 1946, Prentice-Hall, Inc., p. 367.
20. Sewell, William H.: The Construction and Standardization of a Scale for the Measurement of the Socio-economic Status of Oklahoma Farm Families. Stillwater: Oklahoma Agricultural and Mechanical College, Agricultural Experiment Station, Technical Bulletin No. 9, pp. 7-18, 1940.
21. Crump, E. P., Wilson-Webb, C., and Pointer, M. B.: Prematurity in the Negro Infant, Am. J. Dis. Child. **83**: 463, 1952.
22. Taff, M. A., and Wilbar, C. L.: Immaturity of Single Live Births According to Weight With Particular Reference to Race, Am. J. Dis. Child. **85**: 279, 1953.
23. Cawley, R. H., McKeown, T., and Record, R. G.: Influence of the Prenatal Environment on Post-natal Growth, Brit. J. Prev. Soc. Med. **8**: 66, 1954.
24. Peckham, C. H.: The Incidence of Prematurity and the Effect of Certain Obstetrical Factors, J. PEDIAT. **13**: 474, 1938.
25. Tandy, Elizabeth G.: Infant and Maternal Mortality Among Negroes, U. S. Department of Labor, Children's Bureau, Publication No. 243, p. 34, Washington, D. C., 1937.

SURGICAL TREATMENT OF PYLORIC STENOSIS IN AN INFANT WITH HEMOPHILIA A

J. I. DE BRUIJNE, M.D., S. VAN CREVELD, M.D., AND R. STEENDIJK, M.D.
AMSTERDAM, THE NETHERLANDS
WITH THE TECHNICAL ASSISTANCE OF MISS P. E. GROEN

THE surgical treatment of a hemophiliac always involves great risks. Nevertheless, occasionally surgical intervention is absolutely necessary. According to the concept at present held by most investigators, hemophilia results from the congenital deficiency in the plasma of the antihemophilic factor, which is needed for a normal course of the clotting process. The main problem when operating upon a hemophiliac is to normalize the clotting process during operation and for a sufficiently long time afterwards. It is now known that this normalization of the clotting process is not obtained only by restoration of the clotting time to normal; the prothrombin consumption at clotting must also be brought to normal. According to present concepts, based especially on the observations of Brinkhous and others,[1, 2] the best way to control bleeding in general in a hemophiliac and to prevent hemorrhages after operation is to increase the more or less decreased level of the antihemophilic factor in the blood to a certain value by transfusion of fresh blood. In recent years, several reports have been published on transfusion therapy during and after operations in hemophiliacs and one of us with Hoorweg and Stijn,[3] published such an experience in a hemophiliac in whom partial gastrectomy was necessary.

In this paper we want to give a more detailed description of the therapy used in the operation for pyloric stenosis in an infant suffering from hemophilia A.

Late in the evening of May 21, 1957, a male infant 4 weeks old, was admitted to the Children's Hospital of the University of Amsterdam, with a history of projectile vomiting and weight loss of one week's duration.

The material vomited had the appearance of partly digested formula; it contained no bile and no blood.

The infant, whose birth weight was 3.3 kilograms, and who weighed 2.8 kilograms on admission, was severely dehydrated and moderately malnourished; he had a weak cry. Gastric peristalsis was noted over the upper part of the abdomen, and a pyloric "tumor" was felt on deep palpation of the abdomen.

As the history was taken from a relative of the infant's father, no definite information could be obtained about any possible hereditary diseases in the family of the mother. There was none in the father's family.

During the night, 375 ml. of 5 per cent dextrose in water and 125 ml. of 0.9 per cent NaCl were administered subcutaneously. The next morning a blood count showed normal values for hemoglobin content, red cells, white cells, and platelets, but a severe

From the Department of Pediatrics, University of Amsterdam.

electrolyte disturbance was found: plasma sodium 110 mEq. per liter; plasma potassium 3.5 mEq. per liter, and plasma HCO_3 33 mEq. per liter. An attempt to correct this condition was made by the intravenous administration of 250 ml. of 0.9 per cent NaCl, 250 ml. of 5 per cent dextrose in water, to which 10 mEq. of KCl had been added. During this infusion the infant's condition improved perceptibly.

The conclusion was drawn that the patient suffered from hemophilia A. A few hours later the mother came to visit the child and mentioned that a brother of her mother had died of hemophilia 30 years before. On further inquiry, more information was obtained (Fig. 1).

Originally it had been planned to operate on the infant the next day in order to relieve the severe pyloric stenosis. In view of the findings, however, the operation was postponed. The child was given 50 ml. of typed and cross-matched fresh whole blood; 2 hours later the clotting time of the venous blood was 14 minutes and a determination of the amount of antihemophilic factor present in the plasma gave a result of 40 per cent (Langdell and others[2]). This showed that the disturbance of the clotting mechanism could be corrected at least for a few hours. Subsequently a cut down was done in order to be prepared for an emergency and to make parenteral feeding possible. This became necessary since even small feedings which were given together with an orally administered spasmolytic agent consisting of Eumydrin and papaverine did

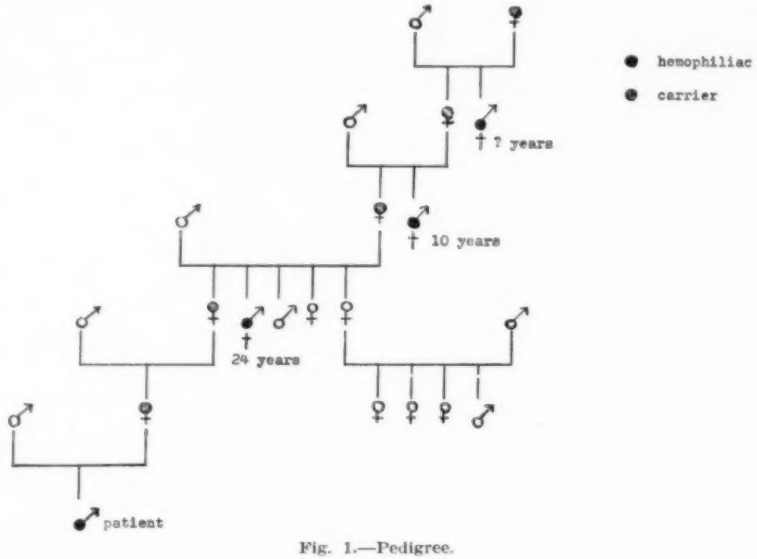


Fig. 1.—Pedigree.

In the meantime it was discovered that the patient still bled slightly from two heel punctures which were made 5 hours previously to obtain the necessary blood for analysis. This induced us to make a study of the clotting mechanism. We found a whole venous blood clotting time (Lee and White) of 50 minutes (e.g., highly prolonged); the prothrombin time (Quick) was normal but the value for residual prothrombin was very high (229 units); a thromboplastin generation test was abnormal and in favor of the diagnosis hemophilia A, and plasma of the patient did not correct the prolonged clotting time of a patient suffering from hemophilia A.

not influence the vomiting. The child continued to vomit copious amounts after almost every feeding and practically no feeding was retained. The vomitus now contained considerable mucus and hematin and it was supposed that gastritis had developed.

The general condition of the infant did not warrant a further delay of surgical treatment, and it was decided to perform a pyloromyotomy on May 24, 60 hours after admission.

pyloromyotomy according to Fredet-Rammstedt was performed by Dr. J. G. Kopp.* Great care was taken to ligate or electrocoagulate all bleeding points. There were no surgical complications.

Following the operation, the transfusion of blood was continued as a slow intravenous drip. The child received a total of 200 ml. As there were no signs of bleeding from the wound, it was felt that more blood might overload the vascular system, and therefore

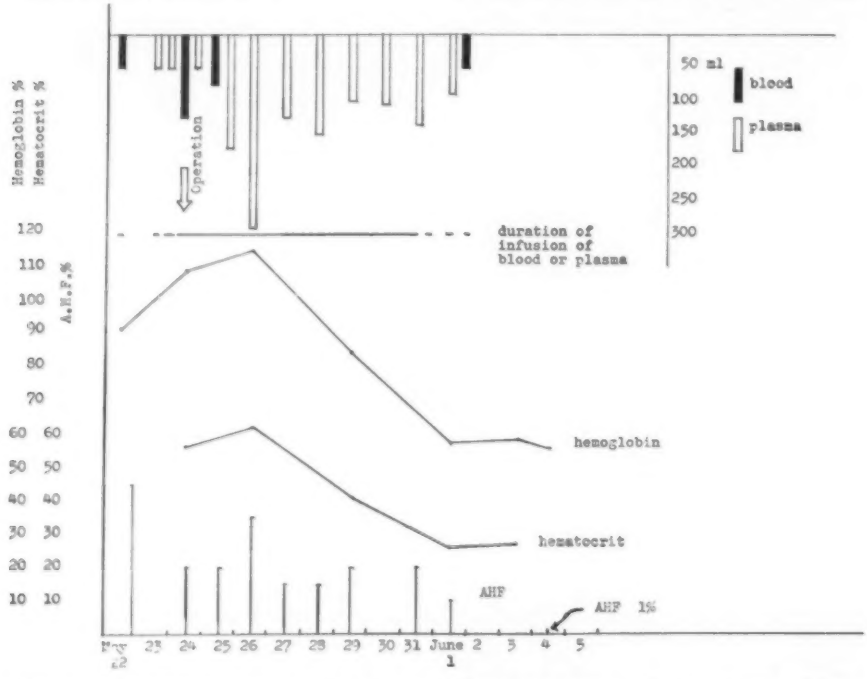


Fig. 2.—Correlation between level of amount of blood and plasma given and antihemophilic factor activity of the patient's blood.

During the night preceding the operation oral feedings were omitted and 100 ml. of lyophilized dried citrated plasma was given intravenously. One hour prior to the operation a transfusion of freshly obtained, typed, and cross-matched whole citrated blood was started.

The operation was done under local anesthesia. The pyloric canal was prolonged and greatly thickened. A

only blood plasma was given (Fig. 2) in order to keep the antihemophilic factor (AHF) at satisfactory levels. Here we assumed that the danger of overloading in using plasma was less than in using whole blood.

Although no food was given orally, the child continued to vomit large amounts of mucus and hematin the

*Surgical department of the University of Amsterdam.

first days after operation. At certain times the vomiting was projectile in character. There were two possible explanations for this occurrence. Either the gastric mucosa was swollen due to the gastritis, resulting in a closure of the pyloric canal, or blood had accumulated in the cut wound in the pylorie sphincter as a result of which the pylorus had closed up again. We were inclined to accept the first of these possibilities as the more likely one because there were no signs of hemorrhage and the amount of AHF in the plasma of the infant, which was checked daily, was kept at a level which supposedly was high enough to prevent bleeding (Fig. 2). The method used for the determination of AHF was that of Langdell, Wagner, and Brinkhous.[2]

The stomach was rinsed out several times, but there was no improvement in the condition until May 28, when the vomitus ceased to consist of mucus and hematin and instead contained small amounts of bile, which proved that the pyloric canal was patent. Very small feedings, consisting of 5 ml. every 3 hours of a solution of 5 per cent glucose, were started. On May 31, 6 days after the operation, vomiting, which had decreased in frequency during the preceding 2 days, ceased, and small feedings with breast milk were started and were progressively increased in amount. On June 3, 10 days after the operation, complete oral feedings with buttermilk were re-established; intravenous therapy was stopped during the preceding day.

Three days after the last transfusion of plasma the antihemophilic factor had dropped to less than 1 per cent, but the child showed no symptoms of hemorrhage.

On May 27, the child had become slightly icteric. This jaundice increased during the following day when the total serum bilirubin level was 4.2 mg. per 100 ml. Apparently a hemolytic reaction had developed due to antibodies present in the plasma administered. To verify this assumption, a Coombs test was done on June 4, when the jaundice had largely subsided again. It was found to be slightly positive, and, in addition, a small titer of immune anti-A antibodies were found in the serum.* (The infant's blood group was A, Rh positive.) The hematocrit value, which was 62 on May 26, fell to 26 on June 1, and the hemoglobin content dropped during the same days from 115 per cent to 57 per cent (Fig. 2). To prevent the infant's becoming anemic, a small transfusion was given on June 1. From that time, no further decrease of the hemoglobin content took place, and the general condition remained good.

DISCUSSION OF TREATMENT WITH BLOOD AND PLASMA

In order to establish an efficient treatment of a hemophiliac during and after operation, it is necessary to consider several questions.

a. What level of AHF in the blood is necessary to prevent bleeding from operation wounds?

b. How long does AHF of transfused blood or plasma remain present in the blood of the patient?

c. What form of therapy is the best, blood or plasma or AHF? Should blood and plasma be fresh or stored? In case of plasma, should it be lyophilized?

d. How much of these substances has to be given to reach and maintain the minimum level of AHF in the blood required to prevent hemorrhages?

e. How long should the administration of AHF to the patient be continued?

The following answers have been given:

a. According to Brinkhous and others[1] a level of AHF of 5 per cent is often sufficient to control hemorrhages, but it may be 15 to 20 per cent of normal (or even higher), especially

*Our thanks are due Dr. J. J. van Loghem, Director of the Central Laboratory of the Dutch Red Cross.

when a prolonged bleeding or tissue destruction has already taken place. Biggs and MacFarlane[7] suggest that even much higher percentages are required to prevent bleeding after operations. In our patient there had been no serious bleeding prior to, during, or after the operation.

b. The fate of the injected AHF is that half of it is lost in approximately four hours (Alexander[4]). This means that even a large transfusion given on the day before operation, as has been done in some cases, has no therapeutic value. Further, it means that it is better to give frequent transfusions than large transfusions once or twice a day. Even better is a continuous infusion in the form of a slow intravenous drip. Our experiences point in the same direction (van Creveld, Hoorweg, and Stijn[3]).

c. In answer to the question, which is best, blood, plasma, or AHF, fresh or stored, all investigators agree that in stored blood AHF has only a short life. Brinkhous and others found that plasma, freshly collected and promptly frozen at –20° C., lost AHF in the first two weeks at about the same rate as stored blood. It is also known that provisionally the AHF content of AHF preparations of human blood may vary greatly. The same holds true for lyophilized plasma. Moreover, infusion of large amounts of AHF has the potential danger of causing serum hepatitis. Attempts to make use of more potent AHF preparations of animal origin[5, 6] provisionally meet practical difficulties (Biggs and MacFarlane[7]). Thus it seems best to give fresh blood or plasma or, when this is not possible, stored blood or plasma which is not older than one week.

d. The quantity of AHF to be given will depend on the AHF content of the donor's blood or plasma, on the AHF content of the patient's blood before operation, and on his condition directly before and after the operation. But even considering all these points, since the critical level under which the danger of bleeding exists is not exactly known, the amounts of blood or plasma or AHF to be given will in part have to be determined empirically. Brinkhous succeeded in preventing bleeding in a boy of 13 months by transfusing 37 ml. per kilogram of body weight every 4 hours. In our patient this would have been 90 ml. blood or plasma in 24 hours. As is seen in Fig. 2, we gave more. This was done in the first place because of the uncertainty, already mentioned of whether the minimum hemostatic level of AHF had to be 5 per cent or higher, and in the second place because of the fact that the AHF of the blood from the donors was unknown and possibly not 100 per cent. We succeeded in keeping the AHF content of the blood between 10 and 20 per cent, and this level seems advisable in most cases of operations upon hemophiliacs. In our anxiety not to give too small amounts of AHF it is probable that we gave on several days more blood and plasma than was strictly necessary. However, at no time did the patient show even slight symptoms of overloading of the circulation. Moreover, repeated determination of the plasma protein content gave no abnormally high values.

e. As regards the question of what length of time the minimum level of AHF required for hemostasis should be maintained, in the course of years we came to the conclusion that after operations of any significance this should be approximately ten days.

In our case the maintenance of fluid and electrolyte balance presented a few difficulties. To prevent hemorrhage it was necessary to establish a continuous intravenous infusion of fresh whole blood or plasma during the first ten days after the operation. In addition, fluids had to be given along the same route. Infants, operated on for pylorospasmus, are not given routine intravenous fluids in our hospital. From 24 hours after the operation small oral feedings are started and gradually increased in amount every day, until, after about 5 to 7 days, complete oral feedings are resumed. In the meantime, the remainder of the necessary fluids is given subcutaneously. In

this case, however, we preferred to refrain from a subcutaneous drip because it might provoke a hemorrhage into the subcutaneous tissues. The infant had received 500 ml. of fluids subcutaneously shortly after admission before we knew that he suffered from hemophilia; this was tolerated remarkably well since only a faintly bluish spot showed the site where the fluid had been given. But we felt that it was undesirable to repeat this. Moreover, as the child continued to vomit after the operation for an unusually long time, fluids had to be administered parenterally for a longer time than was expected originally, and calories had to be included.

During the 10 days between the operation and June 3, the infant was fed intravenously with solutions of 10 per cent invert sugar and of 5 per cent dextrose in water with daily increments of about 20 mEq. of NaCl and 10 mEq. of KCl. The total amount of fluid administered per day was 800 to 900 ml., in addition to which 100 to 150 ml. of dried lyophilized plasma was given daily. The total amount of plasma administered was 1,200 ml.

Immediately before the operation the infant's body weight was 3.2 kilograms; 10 days after the operation it was 3.3 kilograms. There was no dehydration, plasma electrolytes were within normal limits, and the nutritional status was entirely similar to that on admission. On resumption of oral feeding, there occurred no major gain or loss of weight during the first few days. Although no balance studies were done, we concluded from these facts that balance of fluids and electrolytes had been maintained during these 10 days.

There was no abnormal elevation of the total protein content of the serum in spite of the large amounts of plasma given. Blood and plasma volume were not determined, but there were never any signs indicative of overloading of the vascular system. The conclusion that the plasma proteins had been broken down and used as calories was justified in our opinion.

The number of calories given as invert sugar, dextrose, and plasma averaged 230 per 24 hours. This must have been just enough to prevent the infant's losing weight.

SUMMARY

The surgical treatment of a case of pyloric stenosis in an infant suffering from hemophilia A is described. All measures taken before and after operation to prevent bleeding are communicated in detail. The necessity of giving slow continuous infusion of whole blood or plasma, guided by estimation of AHF in the patient's blood, for approximately ten days after operation is stressed.

REFERENCES

1. Brinkhous, K. M., Penick, G. D., Langdell, R. D., Wagner, R. H., and Graham, J. B.: A. M. A. Arch. Path. **61**: 6, 1956.
2. Langdell, R. D., Wagner, R. H., and Brinkhous, K. M.: Proc. Soc. Exper. Biol. & Med. **88**: 212, 1955.
3. van Creveld, S., Hoorweg, P. G., and Stijn, R. W.: Nederl. tijdschr. geneesk. **100**: 3345, 1956.
4. Alexander, B.: New England J. Med. **252**: 432, 484, 526, 1955.
5. MacFarlane, R. G., Biggs, R., and Bidwell, E.: Lancet **1**: 1316, 1954.
6. Bidwell, E.: Brit. J. Haemat. **1**: 35, 386, 1955.
7. Biggs, R., and MacFarlane, R. G.: Human Blood Coagulation and Its Disorders, ed. 2, Oxford, England, 1957, Blackwell Scientific Publications.

SPORADIC CRETINISM WITH GOITER OCCURRING IN IDENTICAL TWINS

HENRY F. FRIERSON, M.D., JOHN C. HAWK, JR., M.D., AND MARGARET Q. JENKINS, M.D.
CHARLESTON, S. C.

A REVIEW of the literature reveals no cases of sporadic cretinism occurring in identical twins, although there is a distinct familial tendency to goitrous cretinism. The purpose of this paper is to present the occurrence of this abnormality in identical twins.

Cretinism encountered in areas where goiter is not endemic is known as sporadic cretinism.[3] It is usually of the athyrotic type and not associated with goiter. This type of cretinism is rarely familial. Cretins with goiter, however, are rarely found in nonendemic areas. There is a high familial incidence of this type of hypothyroidism, suggesting that there is a genetically transmitted defect in thyroid metabolism, but this does not represent any known type of Mendelian inheritance.[1]

Osler reported seven goiters among sixty cases of long-untreated sporadic cretinism in nongoitrous areas in the United States. Wilkins, Clayton, and Bergthrong[1] in their excellent review of the subject collected thirty-two cases in the literature and added two of their own. Sexton and Mack[2] reported five of ten siblings who were cretins, in whom three had goiter and two did not.

Sporadic cretinism with goiter represents a paradox. There is no lack of thyroid tissue and no lack of iodine, but still there is a lack of thyroid hormone. This is thought to be due to an inability of the gland to produce thyroxine.[5, 6, 9, 10, 11] The lack of circulating thyroxine results in an intense hypertrophy of the gland.[4, 8] Hypothyroidism may exist for many years before the goiter develops, and the gland may become enlarged any time from infancy to adult life.[7]

South Carolina can hardly be considered an endemic goiter area; in fact, it is sometimes called the "Iodine State."

CASE REPORTS

Jan and Joy B., identical twins, were admitted to Roper Hospital, Charleston, South Carolina, through the Medical College of South Carolina Cancer Clinic, on Oct. 7, 1955, because of a mass in the neck of each child. The children were born in Sumter, South Carolina, on June 20, 1955, approximately six weeks prematurely, with Jan having a birth weight of 3 pounds 13 ounces, and Joy weighing 3 pounds 5 ounces. They were placed in Isolettes and did well. At about 2 weeks of age, Jan had one rather severe episode of cyanosis which responded to additional oxygen and did not recur. The children were kept in

From the Departments of Surgery and Pediatrics, the Cancer Clinic of the Medical College of South Carolina, and the Roper Hospital.

This study was supported in part by an Undergraduate Training Grant from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service, Bethesda, Maryland.

the hospital until each weighed about 5 pounds and were then discharged. Around the middle of September, 1955, each child was noted to have a mass in the right side of her neck. Jan had a mild cough and hoarseness at that time. Chest and neck x-rays were negative. In about two weeks her hoarseness had increased, her cough had become more persistent, and she took her formula poorly. She had lost from 7 pounds 2 ¾ ounces on September 21, to 6 pounds 10 ounces on October 5.

Joy had also developed a mass in her neck about the same time as Jan. This mass was located in the region of the lower portion of the sternocleidomastoid muscle on the right side. This was more prominent on increased intrathoracic pressure due to straining or crying. She was having less respiratory symptoms than her sister. Both children had received a formula and vitamins.

Family History.—The father was 46 years of age and in good health except for chronic bronchitis. The mother was 38 years old and had asthma, hay fever, and allergy to dogs, but otherwise was in good health. The couple had been married sixteen years and there had been two previous pregnancies, both of which ended in miscarriages. The paternal grandfather had had a 27-pound benign tumor (probably lipoma) removed from his chest wall. Family history was otherwise negative. The mother had taken no antithyroid drugs and there was no history of ingestion of foods sometimes considered goitrogenic, such as cabbage or soybeans.[8]

Physical Examinations.—

Jan: Weight was 6 pounds 10 ounces; length, 47.5 cm.; head 35.5 cm.; chest 32 cm. Respirations were 42 and pulse 164. The child was in minimal respiratory distress, with some inspiratory and expiratory stridor. The tongue was prominent. There was a 3 by 4 cm. soft, somewhat cystic, freely movable mass over the region of the mid and lower sternocleidomastoid muscle on the right side. There was no pulsation, but the mass increased in size on crying. There was questionable slight ptosis of the right eyelid. There were several small hemangiomata over the body. The remainder of the physical examination was normal.

Joy.—Weight was 8 pounds; length 50 cm.; head 36 cm.; chest 35 cm. There was no respiratory distress. The tongue was big, and the floor of the mouth seemed elevated. There was a mass similar to Jan's in the same location in the right side of the neck in the region of the mid-portion of the sternocleidomastoid muscle. The remainder of the physical examination was normal.

A barium swallow on Jan revealed a moderate prominence of the soft tissues in the posterior aspect of the oropharynx. The tongue appeared relatively large in size. The study was otherwise essentially negative.

The children were thought to have cystic hygromas and were discharged to be readmitted to the hospital for operation at a later date.

Following discharge from the hospital, the children did well at home, with the masses appearing to regress in size until approximately the last week in November, when they again began to enlarge. The children were readmitted on Dec. 12, 1955, with operation being contemplated on the following day. Jan now weighed 7 pounds 9 ounces, and still had some stridor. There was

TABLE I. LABORATORY DATA

	HB.	R.B.C.	W.B.C.	POLYS.	LYMPHS.	MONOS.	BASOS.
Jan:	12.5	4.34	9,900	52	46	2	–
Joy:	12.0	4.45	7,440	55	41	2	2

Urinalysis

Jan: yellow, acid; 1.011; alb. 0; sugar 0; W.B.C. 6-12; R.B.C. 0; casts fine, granular
Joy: clear, acid; 1.004; alb. 0; sugar 0; R.B.C. 0; casts 0

slight cretinoid facies, the tongue was big and thick, and the floor of the mouth was elevated. The mass in the neck extended from the ear to the supraclavicular region and appeared to extend across the midline but was relatively small on the left side. It measured 4 cm. in the right side. (Fig. 1.)

The children were completely reevaluated on Dec. 15, 1955, and at this time the neck masses were thought definitely to extend across the midline. The facies were suggestive of cretinism, and the tongues were slightly thick. Therefore, thyroid studies were obtained. Jan had a blood cholesterol

Fig. 1.

Fig. 2.

Fig. 1.—Jan B. at the age of 6 months. Note fullness in the neck and cretinoid appearance.
Fig. 2.—Joy B. at the age of 6 months. Neck fullness is increased on increased intrathoracic pressure produced by crying.

The floor of the mouth was also elevated in Joy, and she had an almost identical mass. (Fig. 2.)

Routine laboratory studies were still normal in both children. Both serologies were negative. X-rays revealed a soft tissue mass in the posterior pharynx on Joy, and a prominence of the soft tissues in the neck, posterior to the esophagus, in Jan.

Operation was scheduled for Jan for Dec. 13, 1955, but was canceled due to laryngospasm and difficulty in intubation at the time of induction of anesthesia.

of 166 mg. per cent, a protein-bound iodine of 3.0 meg. per cent, and radioactive iodine retention of 41 per cent at 24 hours. Joy had a blood cholesterol of 125 mg. per cent, a protein-bound iodine of 2.4 meg. per cent, and a I^{131} retention of 35 per cent at 24 hours.

An aspiration biopsy of the neck mass was performed on Jan on Dec. 16, 1955, and this was reported as thyroid and adipose tissue. There was follicuoid arrangement but no well-developed acini or colloid, and the cells were foamy or granular.

With this additional information at hand, it was decided that the children were definitely goitrous cretins, and they were therefore started on thyroid extract, ¼ grain per day on Dec. 20, 1955. This was well tolerated and was increased to ½ grain per day on Dec. 21, 1955, and ¾ grain per day on Dec. 22, 1955. They were discharged on this dosage on Dec. 26, 1955. The twins were followed closely by their referring pediatrician and were not seen again until Oct. 17, 1956, at which time they were both doing extremely well. (Fig. 3.) They had been taking their thyroid medication regularly, and each weighed 18½ pounds. According to the mother, the neck masses had completely disappeared within one month after therapy was started, and they had had no respiratory difficulty. Both children had been walking since the age of 12½ months, and started talking at one year. They were both alert, active, and energetic. Each had seven teeth and the fontanels were open. They were eating well, taking vitamins, and were on an evaporated milk formula.

At this time the serum cholesterol (initial cholesterol determination had been on whole blood) was 203 mg. per cent on Jan and 161 mg. per cent on Joy. Protein-bound iodine on Jan was 3.7 meg. per cent, and on Joy 3.0 meg. per cent. The normals in our laboratory are 4 to 8 meg. per cent.

In view of the fact that the protein-bound iodine determinations were still below normal, it was thought advisable to increase their dosage of thyroid extract. This was increased to 1 grain per day.

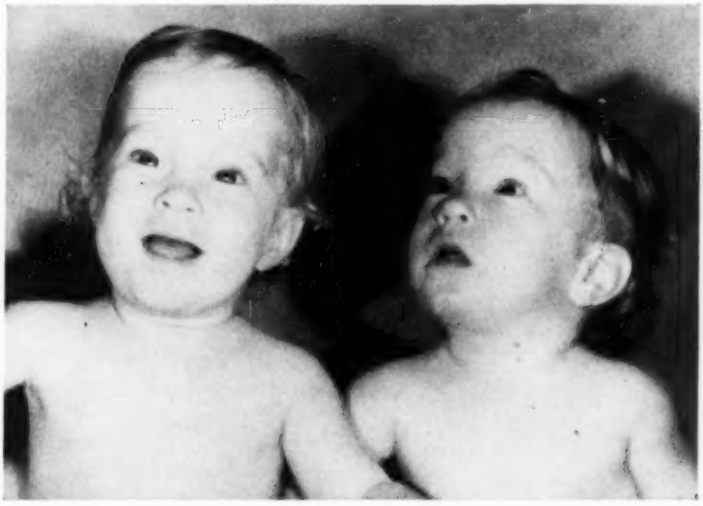


Fig. 3.—Joy B. (left) and Jan B. (right) at the age of 16 months.

The children were last seen on May 4, 1957, at which time both were still doing well. Each twin weighed 22 pounds. They were active, talking, eating well. The fontanels were closed, and they apparently were having normal growth and development.

SUMMARY

Identical twins with sporadic cretinism with goiter are presented. These children at first were erroneously thought to have cystic hygromas of the neck. They have responded well to

treatment with desiccated thyroid extract, and their neck masses have disappeared completely.

Although rare, sporadic goitrous cretinism does occur and should be included in the differential diagnosis of neck masses in infancy and childhood so that appropriate studies may be obtained, diagnosis made, and treatment instituted early.

REFERENCES

1. Wilkins, L., Clayton, G. W., Jr., and Bergthrong, M.: Pediatrics 13: 235, 1954.
2. Sexton, D. L., and Mack, R.: J. Clin. Endocrinol. 14: 747, 1954.
3. Stanbury, J. B., Ohela, K., and Pitt-Rivers, R.: J. Clin. Endocrinol. 15: 54, 1955.
4. Stanbury, J. B.: J. Clin. Endocrinol. 11: 740, 1951.
5. Stanbury, J. B., and Hedge, A. N.: J. Clin. Endocrinol. 10: 1471, 1950.
6. Silverman, S. H., and Wilkins, L.: Pediatrics 12: 288, 1953.
7. Jackson, A. D. M., A. M. A. Arch. Dis. Childhood 29: 571, 1954.
8. Lerman, L., Jones, H. W., and Calkins, E.: Ann. Int. Med. 25: 677, 1946.
9. Hamilton, J. G., Soley, M. H., Reilly, W. A., and Eichorn, K. B.: A. M. A. Am. J. Dis. Child. 66: 495, 1953.
10. Hubble, D.: Lancet 1: 1112, 1953.
11. McGirr, E. M., and Hutchison, J. H.: Lancet 1: 1117, 1953.

INFANT AND CHILD MORTALITY IN A KOREAN RURAL AREA

DUK JIN YUN, M.D., M.P.H.*
SEOUL, KOREA

INTRODUCTION

WE OF the Korean medical profession have been concerned for a long time about obtaining accurate statistics as to the health of the people. Due to social conditions and the present health organization it has not been possible to obtain accurate vital statistics. Routine reporting of births and deaths is inadequate, and when deaths are reported the medical certification of cause is unreliable. The latter is due to the fact that Korea has two kinds of doctors who are allowed to write prescriptions and death certificates. One is the medical school graduate and the other is the so-called "Chinese herb doctor," who has not graduated from medical school but has passed the national herb doctor examination. Chinese original medicine, which was imported to Korea from China many thousand years ago, was employed until modern medicine was imported from the West. The herb doctors, who are allowed to use herb medicine, do not know modern medicine and cannot make an accurate diagnosis. In Korea the doctors are about equally divided between the two groups. Many people do not consult either type; of those who do, however, more use the herb doctor, as a result of ignorance and because he is less expensive.

Although improvement in statistics* and medical care was taking place, it was my firm opinion that we could not wait for satisfactory data to be developed. I therefore undertook the investigation here reported to obtain some idea of the infant and childhood mortality in a single Myon, which is the smallest administrative unit in Korea, with about 10,000 population. The data do not represent Korean infant and childhood mortality as a whole, but only in a Korean rural area.

Before presenting the study and its findings some general background information concerning Korea and the particular Myon selected for study, Kaijung-Myon, may be of interest.

HISTORICAL NOTE AND DESCRIPTION OF KAIJUNG-MYON

Prior to 1945 when Korea obtained freedom from Japan, 80 per cent of the farmers were tenant farmers to the Japanese landowners, and 40 per cent of the farmers as well as 40 per

From the Institute for Rural Health, Kaijung-Myon, Okku-Gun, Chulla-Book-Do, Korea.

*Present address: Department of Pediatrics, Severance Medical School, 5-Ka, Namdaimoon-Ro, Choong-Koo, Seoul, Korea.

*An investigation about the life of Jeju island people was done in 1943 by J. M. Suk.[1] Dr. VanBuskirk[2] investigated the infant and child death in Seoul in 1925. Dr. Mizushima made the first abridged life table for 1926-1930, and Dr. Choi[3] made a second life table, this one unabridged. In making the life tables of Korean people, however, they recognized that the recorded number of deaths of infants and children was too small. Dr. Harafuji[4] did not make an effort to estimate these early rates and made a life table of each province of Korea based on the number of deaths of those over 5 years of age.

cent of Kaijung belonged to Mr. K., a large landowner, who established a dispensary which furnished medical treatment without charge to his tenants. Therefore, from 1935 to 1944, about 40 per cent of Kaijung-Myon people were able to consult a physician without charge. The farm rent at that time was 60 per cent of all harvests. The landowners were taxed for land and water, while the tenants bore the expenses of fertilizer and farming. In 1946, all of the land which had belonged to the Japanese landowners, about 80 per cent of the total land, was taken over by the New Korean Company established by the American Military Government. From 1946 to 1947, the tenants gave one-third of their total harvest to the New Korean Company, and bore all the taxes and expenses involved. In 1948 all acreage was returned to the Korean Government and land reform was instituted. The land was to belong to the farmers, who had to pay 30 per cent of the total harvest to the Korean Government for five years to pay for the land. In addition, other taxes, which include income tax and a tax for irrigation water, add 30 to 40 per cent to the fixed expenses of the farmer.

Kaijung-Myon is situated in Chulla-Book-Do, 6 kilometers from the city of Kunsan, which has about 100,000 population. The size of Kaijung-Myon is 4,200 acres, consisting of about 2,650 acres of rice paddy, 400 acres of dry firm field, 1,000 acres of forest, and 150 acres of house lot. The population was about 10,000, with 1,618 families, 90 per cent of them living on farms. The farms average about 2 acres for each family, with only about 10 per cent being larger than 3 acres. This is a smaller average than in any other country, and about one-half acre per family smaller than in Japan. The average family size is 6.1, with 25 per cent of the families above 7 in number, and 5 per cent above 10; at the lower end, 25 per cent are below 5, and 5 per cent are below 3.

MATERIALS AND METHOD

Kaijung-Myon was selected for a maternal and child health program which was to be initiated in 1954. It was decided, therefore, to obtain certain basic health data immediately before the start of the program. These data, some of which are reported here, were obtained during the last week of December, 1953.

During this week, each home in the Myon was visited and an investigation card was completed which had been designed for the purpose. Information obtained included the following: list of those living in the household, their age, sex, marital status, and relationship to the head of the household; for each married female, a list of all births, including fetal deaths, indicating date of birth, order of births, weaning history, and date of death if not surviving to date of investigation; a listing of all other births and deaths occurring in the household in the last thirty years, giving date of birth or death, and age at death. The weaning history was sought for all births. In the case of deaths, inquiry was made concerning the medical care obtained prior to death and the cause of death. Seventy-five per cent of the deaths

had taken place without any medication or consultation with a doctor, so that in this investigation the cause of death in at least 75 per cent of deaths is purely presumptive, based on onset, duration, and symptoms reported. In the analysis, care was taken to avoid duplication, such as could occur, for example, when a child of a married woman in one household is married and living in another household in the same Myon at the time of the investigation.

The study was headed by two doctors, a pediatrician and an obstetrician. The interviewing itself was done by 40 third-year students of a public health nursing school. The public health nursing students were instructed in advance for about 30 hours as to how to obtain accurate answers from the rural women. Before the investigation the women of Kaijung-Myon were instructed through special meetings to stay home on the day selected for the visiting of their particular area, and to cooperate with the investigation. The public health nursing students visited each home, queried each married woman in accordance with the investigation card, and recorded the answer.

This system, even with complete reporting by all households, leads to some deficiency in reporting of births and deaths among those households no longer in the Kaijung-Myon due to death or migration. Because of the way households are established and maintained and because migration from this Myon has been small, the error thus introduced is probably slight.

RESULTS AND DISCUSSION

Estimates of the population, birth rate, death rate, and rate of natural increase are shown in Table I for five recent years.

The population was estimated for the end of each year by successive subtractions of births and additions

TABLE I. POPULATION, LIVE BIRTHS, DEATHS, AND ANNUAL RATES PER 1,000 POPULATION FOR LIVE BIRTHS, DEATHS, AND NATURAL INCREASE, BY YEAR, 1948-1952, KAIJUNG-MYON, KOREA

YEAR	ESTIMATED MIDYEAR POPULATION	LIVE BIRTHS	BIRTH RATE	DEATHS	DEATH RATE	RATE OF NATURAL INCREASE
1948	8,516	302	35.5	150	17.6	17.9
1949	8,702	338	38.8	118	13.6	25.2
1950	8,898	331	37.2	160	18.0	19.2
1951	9,049	283	31.3	152	16.8	14.5
1952	9,212	346	37.6	150	16.3	21.3

TABLE II. FETAL AND INFANT MORTALITY, BY YEAR, 1948-1952, KAIJUNG-MYON, KOREA

YEAR	INFANT DEATHS	INFANT DEATH RATE*	FETAL DEATHS	FETAL DEATH RATIO†	LIVE BIRTHS
1948	51	168.9	24	79.5	302
1949	29	85.7	19	56.2	338
1950	29	87.6	28	84.6	331
1951	34	121.4	32	113.1	283
1952	32	92.5	29	83.8	346

*Infant death rate—Infant deaths in the year per 1,000 live births in the same year.
†Fetal death ratio—Fetal deaths in the year per 1,000 live births in the same year.

of deaths, starting with the population counted in the study. The mid-year population was then taken as the arithmetic average of the population estimates for the beginning and end of each calendar year.

The birth rates are fairly high and range from 31.3 to 38.8 with no apparent trend. In Korea there has been no program of birth control or artificially induced abortions by which the birth rate in Japan fell to 23.4 in 1952 and is decreasing gradually.[5, 6] The relatively low birth rate in 1951 is considered to be due to the Civil War in Korea. The crude death rates were fairly high, ranging from 13.6 to 18.0, again without trend. The death rate in Japan was 8.9 in 1952.

According to Table II, the fetal death ratio and the infant death rate are extremely high; and for these years there is no apparent trend in either series of figures. The highest fetal death ratio in Kaijung-Myon was in 1951 during the Civil War in Korea. The fetal death ratio in Japan in 1952 was 92.3, but artificially induced abortions were not included. The infant mortality rate in Japan in 1952 was 49.4.

Table III shows cause of infant deaths for all those reported to this study for the previous thirty years. As stated before the cause of death is based on the mothers' explanations of their babies' symptoms before death. It is probable that there is an increasing deficiency of reported births and deaths with the length of period prior to the investigation. However, examining the causes by single calendar years revealed no outstanding trends, except as noted below. Therefore, in order to give some stability to the distribution of cause of death the combination of the thirty-year experience is used.

The term, congenital weakness, is not a diagnosis. The reason for using it is that most mothers said that the baby was very weak and small and could not suck well, without giving other striking symptoms of disease. The heading "Congenital weakness"

TABLE III. THE ESTIMATED CAUSES OF DEATH IN BABIES UNDER 1 YEAR, BY AGE, FOR PERIOD 1924-1953, KAIJUNG-MYON, KOREA

CAUSE OF DEATH	AGE				TOTAL	PER CENT
	WITHIN 1 WEEK	1 WEEK-1 MONTH	2 MONTHS-6 MONTHS	7 MONTHS-12 MONTHS		
Congenital weakness	144	27	15	7	192	22.2
Convulsion	6	14	39	37	96	11.1
Diarrhea and enteritis	--	6	16	54	76	8.8
Erysipelas	11	34	14	12	71	8.2
Measles	--	--	21	43	64	7.4
Smallpox	--	--	24	35	59	6.8
Pneumonia	--	8	18	30	56	6.5
Tetanus	36	19	1	--	56	6.5
Bronchitis	3	5	15	18	41	4.7
Malnutrition	--	3	12	10	25	2.8
Pertussis	--	--	12	10	22	2.5
Dysentery	--	--	4	14	18	2.1
All others*	14	6	18	18	56	6.5
Unkown	3	7	12	13	35	3.9
Total	217	129	221	301	867	
Per cent	25.0	14.9	25.5	34.6		100.0

*All others include birth injury, septicemia and pyemia, meningitis, accident, congenital malformation, congenital syphilis, diphtheria, etc.

probably includes prematurity, postnatal asphyxia, atelectasis, some birth injuries, blood dyscrasias, congenital heart disease, and other diseases of the neonatal period. Convulsion also is a symptom, not a diagnosis. The causes vary; however, those with fever, vomiting, stiffness in the neck indicating possible meningitis, and encephalitis are not included. Probably included are subdural hematoma due to birth injury or other trauma, tetany, hypoglycemia, epilepsy, and other hypoxia.

Congenital weakness and convulsion, the cause of one-third of the infant deaths, might not be relieved by the limited equipment in Korean rural dispensaries. However, the remaining causes of infant mortality, mainly infectious, might be relieved or prevented by taking adequate measures even with our limited equipment. Diarrhea and enteritis, appearing third highest, indicate widespread insanitary conditions. Erysipelas, fourth in order, is markedly decreasing since the importation of antibiotics begun in 1945. Measles ranks fifth in order, and smallpox sixth with 6.8 per cent. The majority of the rural Koreans firmly believe that measles and smallpox are brought by the "Evil One," and if treated by a doctor the "Evil One" could become angry and the disease might become worse. Tetanus, ranking eighth in order, and accounting for 6.5 per cent of the deaths, is a characteristic infection in the Korean rural area where the people are so poor that they cannot even consider calling a doctor or midwife to assist in the delivery. In addition, they use unsterilized scissors and thread on the umbilical cord. Instead of using oil paper, the mother and new baby rest on straw in obedience to an ancient custom aimed at concealing the blood associated with birth. The fixed opinion that the newborn infant should not be treated by doctors adds to the incidence of erysipelas and tetanus. Malnutrition is due to a deficiency of breast milk, and when this occurs rural people are too poor to consider artificial feeding

TABLE IV. THE ESTIMATED CAUSE OF DEATH IN CHILDHOOD IN KAIJUNG-MYON, KOREA

CAUSE OF DEATH	AGE (YEARS)				TOTAL	PER CENT
	1	2	3	4		
Measles	101	50	38	30	219	23.2
Diarrhea and enteritis	63	28	26	8	125	13.2
Pneumonia	43	20	35	10	108	11.4
Smallpox	45	20	20	12	97	10.3
Dysentery	35	16	16	16	83	8.7
Convulsions	35	14	12	5	66	7.0
Bronchitis	20	13	14	3	50	5.3
Pertussis	17	9	10	2	38	4.1
Meningitis (non-tuberculous)	10	7	4	8	29	3.1
Malnutrition	5	8	1	3	17	1.8
Diphtheria	9	1	3	2	15	1.6
Tuberculosis (all forms)	6	4	1	1	12	1.3
All others*	23	16	7	13	59	6.0
Unkown	12	5	5	6	28	3.0
Total	424	211	192	119	946	
Per cent	44.9	22.3	20.2	12.6		100.0

*All others include nephritis and nephrotic syndrome, accident, erysipelas, and septicemia and pyemia, etc.

with animal milk. Usually only rice powder is used as a baby food when breast milk is insufficient.

In evaluating childhood mortality in Kaijung-Myon, I will deal with the period of childhood included in ages of 1 through 4 years. This is a period of high mortality and will permit comparison with other countries using this rather common age grouping of early childhood.

According to Table IV, more than 85 per cent of the Korean rural child deaths can be attributed to contagious diseases or to diseases caused by microorganisms. Up to 1945 there had been few deaths from smallpox, but since 1946 there has been a sudden increase in smallpox mortality. Compulsory smallpox vaccination was not performed from 1946 up to 1952 when the biggest outbreak of smallpox in recent years occurred. Another reason is that in 1947 Korean production of smallpox vaccine ceased, and it was imported from America or Japan, usually after an outbreak of the disease.

In reviewing the cause of death in Korean rural children, we find that most of the deaths could be prevented or controlled by application of known methods of disease control.

Because of the close relationship between diet and health at all ages, and particularly among young children, some data are presented concerning feeding and weaning practices. In Korea, few farms own milk cows. On the whole, women must depend on their own breast milk to feed their infants. In the study data were obtained regarding the feeding of 8,536 infants. Ninety-six per cent were reported to have been fed only breast milk up to the time that solids were added. The remainder used cow's milk, gruel with rice, or various combinations of breast milk, cow's milk, and rice gruel. Knowledge of artificial feeding is poor among rural areas, and most of the babies artificially fed die of malnutrition. In weaning from the breast the women do not shift the baby gradually from milk to soft infant diet to adult food, but begin the weaning with adult food. There is no definite weaning period in Korean rural areas. The infants usually remain on breast milk until the mother again becomes pregnant and the milk ceases to flow. Most babies are weaned at the ages of 2 to 3 years; earlier weaning is usually due to a deficiency in the mother's milk or to pregnancy.

The average weaning age found in the study was 2 years and 3 months; about 25 per cent were weaned before 1½ years, and 25 per cent after the age of 3 years. The last infant in a family may continue on breast milk past the age of 5 years. However, when the child becomes 2 years old, he eats everything which adults eat in addition to the mother's milk.

SUMMARY AND RECOMMENDATIONS

During the last twenty years, Korea has labored under many types of unbearable experiences. Her young men and her economy were oppressively mobilized by the Japanese, especially toward the end of World War II. After obtaining freedom from Japan in 1945, the political and economic situation was very unstable. In addition, a Civil War followed, lasting three years, in which 80 per cent of the productive factories were destroyed. The mobilization of young

men by the draft brought enormous loss of life to the country. In addition, several millions of refugees seeking freedom from North Korea have settled in the country. Although the war has now ceased, the Korean people still have a feeling of uncertainty about the stability of the truce. In such an historically miserable background, Kaijung-Myon, as a part of Korea, displays the influence of these experiences.

The findings for this Myon were based on a house-to-house survey carried out in the last week of December, 1953.

The economic condition of Kaijung-Myon, as in other Korean rural areas, is very poor. This poverty reflects the violent variations at the national level. The only difference between Kaijung-Myon and other rural areas is the existence of a fairly large dispensary near by. This dispensary has offered free service to about 40 per cent of the people of Kaijung-Myon since 1935, and since 1949 it has included a 150-bed hospital.

The infant mortality rate of Kaijung-Myon is twice as high as that of Japan. More than 60 per cent of the infant deaths and more than 85 per cent of the deaths of children 1 to 4 years of age in Korean rural area can be attributed to contagious diseases or to diseases caused by microorganisms, which could be largely prevented or controlled by timely adequate measures. Based in part on the findings here reported, the following recommendations are suggested:

1. Economic improvement by reducing the rural population by constructing new factories.

2. Reduction of superstition by more extensive health education.

3. Environmental and health service improvement:

a. Health education of "headman" in family or community.

b. Improvement of water supply, sewage disposal system, and privies to prevent contagions and breeding of flies.

c. Routine vaccination of infants and children for smallpox, pertussis, diphtheria, and tetanus.

d. Continue maximum use of breast feeding, but education in artificial feeding for those mothers needing this resource. Protein supplement by soybean and fish at the time of weaning.

e. Establishment of rural health services and health insurance by the help of the Government.

I am indebted to Dr. Lee Young Choon, Director of Institute for Rural Health in Korea for kindly supporting this investigation. I am also indebted to Dr. Rowland V. Rider, Assistant Professor of the Maternal and Child Health Division, School of Hygiene and Public Health, Johns Hopkins University, for reviewing and correcting this article for presentation.

REFERENCES

1. Suk, Ju Myong: Life Survey on the People of Jeju-Island, Seoul, 1949.
2. VanBuskirk, J. D.: Public Health Problem in Korea, as shown by a Study of Child Mortality. China M. J. 41: 244, 1927.
3. Choi, Eui Young: Life Tables of Korean People, 1931-1935, J. Korean M. Ass. 29: 68, 1939.
4. Harafuji, S.: Life Tables of Korean People by Province, 1934-1936, J. Korean M. Ass. 30: 1, 1940.
5. Ministry of Health and Welfare, Japanese Government: A Brief Report on Public Health Administration in Japan, 1955.
6. Seki, M., Muramatsu, M., and Fukushima, I.: Koshu Eisei Teiyo (Public Health Review), Tokyo, 1952, Igaku Shoin Co.

Clinical Pathological Conference

THE CHILDREN'S MEDICAL CENTER
BOSTON, MASS.

SIDNEY FARBER, EDITOR
JOHN M. CRAIG, ASSISTANT EDITOR

THIS white girl, 7 years and 8 months old, died at home and was brought here for post-mortem examination.

The patient was well until the evening before her death, at which time she complained of headache and malaise. She was thought to have fever. She retired early and awoke at 2:00 A.M., retching, vomiting, and acutely ill. She was said to have had several bowel movements following this. "Purple spots" were seen by the mother, who called the pediatrician at 5:30 A.M. Upon his arrival, twenty minutes later, he found the child mottled, dusky, pulseless, and sparsely covered with petechiae in the skin folds of the groin and neck. No other members of the family were known to have a similar illness. The child was not on prophylactic antibiotics and had received no courses of corticosteroids recently. Earlier in the day she had visited the family dentist. The only medication given to her during this illness had been a few aspirin tablets.

The mother's pregnancy and delivery had been normal except for spotting during the first trimester. The patient was said to have been jaundiced, and remained so until 8 months of age. She developed vomiting at 2 weeks of age, which was diagnosed as pyloric stenosis. She was given medical treatment and the vomiting gradually disappeared by 9 months of age. She was thought by the mother to be pale, weak, and listless for the first few years of life. She had eczema in infancy, measles and mumps at 5 years, and chicken pox at 7 years of age. There were repeated ear infections and a moderate amount of vaginal discharge on occasions. The child was said to have developed bleeding tendency at 3 years of age. At 4 years of age she was seen at a hospital in another city because of this bleeding tendency. No petechiae were found on physical examination, but the spleen was palpable 6 cm. below the costal margin. The platelet count was low. The counts remained low, circa 110,000, on repeated observations, and at 5½ years of age the spleen was removed. The blood group was O, Rh positive, with both the direct and indirect Coombs test negative. The splenic vein was normal at operation and the portal venous pressure was recorded at 200 mm. of water. The spleen was said to have been five times normal in size.

The patient was seen here in April, twenty-two months before death, when a blood count revealed an erythrocyte count of 5.0 million per cubic millimeter, a hemoglobin of 13.2 Gm. per cent, a leukocyte count of 27,000 per cubic millimeter and platelets of 345,000 per cubic millimeter. It was stated that since splenectomy she had had no further trouble with bleeding tendency.

The child came here again ten months before death for a follow-up visit, at which time her physical examination showed a blood pressure of 96 mm. Hg systolic, temperature 99° F., height 93 cm., and weight 36¼ pounds. The child was described as a moderately well-developed, quite obese girl, who was alert and cooperative. Her optic discs were seen by a –3 diopter correction. Tympanic membranes were retracted. Examination of the skin, chest, heart, and abdomen was negative except for healed chicken pox lesions, scar of splenectomy, and a liver edge about 1 cm. below the right costal margin. Neurological examination was normal. Laboratory tests at that time revealed a platelet count of 553,000 per cubic millimeter. No urine could be obtained for examination.

Her last two visits here were eight months before death, for evaluation of her ears, because of repeated bouts of otitis and purulent otorrhea. She was described then as having adenoid facies. There was a foul odor from both ears, without any definite exudate in the canals. Eardrums were retracted and scarred. There was no mastoid tenderness. The tonsils and pharynx were injected, and she had anterior and posterior palpable cervical lymph nodes. It was thought that if she had further trouble, she should return for an adenoidectomy in the fall. She was not seen again until death.

DISCUSSION

DR. CHARLES A. JANEWAY.*—This child was the product of a moderately normal pregnancy, and I say *moderately* normal, because there was bleeding in the first trimester, something we tend to view rather seriously. If this child had a true portal pressure of 200 mm. of water at the operation for removal of her spleen, she did have portal hypertension; hence she presumably had congestive splenomegaly. This may very well have accounted for the thrombocytopenia which is one of the earlier manifestations of hypersplenism, but she did not show any of the other changes, that is, the depression of white or of red cells and hemoglobin, which these patients do show if they have the advanced picture of Banti's syndrome. We have the story, also, of an undiagnosed form of jaundice occurring in the newborn period, and lasting for eight months, followed four years later by splenomegaly and portal hypertension. This certainly suggests that some change took place within the liver of this child, which accounted for the portal hypertension, although I don't see how we can make an accurate diagnosis on the information that we have. This child may have had neonatal sepsis, with a cholangitic type of picture followed by periportal scarring, with the slow development of enough cirrhosis to compromise the portal circulation. She might have had a septic picture with the development of thrombi in some of the major

*Physician-in-Chief at The Children's Hospital, and Thomas Morgan Rotch, Professor of Pediatrics, Harvard Medical School.

portions of the portal vein, which in turn led to portal hypertension. She may have had (and this seems less likely) neonatal hepatitis, with the development of postnecrotic scarring of the liver, postnecrotic cirrhosis and, as a result of this, portal obstruction. With this blood group setup, there is no reason to think that this child had erythroblastosis with subsequent jaundice, and possibly the "inspissated bile syndrome" that we talk about. There was obviously some reason for the child to be taken to another hospital at the age of 4 years, and it seems to have been pallor, weakness, and listlessness rather than a bleeding tendency, as the mother seemed to recall at the time our history was taken.

The rest of this child's history—and the important part of it, I think—is a consequence of the treatment given to the child at this time. What we have is a child, who, subsequent to her splenectomy at the age of 5½ years, has primarily had trouble with infection. There has been a series of episodes with a purulent discharge from the ears, which must have been due to fairly severe otitis media. Furthermore, the physical examination at that time showed her to have adenoid facies and scarring of the drums, which certainly suggests that there was some blocking of her eustachian orifices. There was no mastoid tenderness, but her tonsils and pharynx were injected, and she had lymphadenopathy in the cervical region, all suggesting that she had a series of upper respiratory bacterial infections with extension of the processes to some of the cervical nodes.

A year later, when apparently well, on the day before death she suddenly awoke with headache, malaise, and fever; this was a very rapidly progressive series of symptoms. The child had had none of the medications which sometimes precipitate unexpected infections nowadays, namely antibiotics or corticosteroids. She had been to the dentist in the morning but she had been well enough to go and nothing unusual happened at that time, so far as we know.

This clearly is the picture of overwhelming sepsis in a child.

What type of sepsis did she have? I do not think there is anything here which can give us a hint; she might have had a hemolytic streptococcal, a meningococcal, or a pneumococcal infection. It would not surprise me in the least if she had meningitis, although she may have died too rapidly to develop meningitis; her headache, vomiting, and retching at least suggest this. The diarrhea is certainly not specific. Vomiting and diarrhea are common symptoms at the onset of many acute infections. The petechiae are centainly not diagnostic, particularly when they occur in those locations where pressure from bedclothing performs a "tourniquet test" on the individual. If you look over any group of children with acute infections, such as measles, tonsillitis, or scarlet fever, you will find multiple petechiae, very often at little points of trauma; a very common place is under the armpits where the underwear pinches. You can get a positive tourniquet test quite frequently in scarlet fever. I think it is impossible to say anything except that, in all probability, she had a coccal infection. The reason I say this, is, first, because of the speed with which this developed, and, second, because these are the most common offenders in a child of this age in the season of

respiratory infections and in an individual who has had a lot of ear difficulty. I would believe hemolytic streptococcus is most likely, pneumococcus second, and meningococcus third, but this is pure guesswork.

Where is this infection coming from? Infections in our part of the world, resulting from this group of organisms, usually arise in the respiratory tract unless there is a surgical traumatic lesion in the extremities. Could this have been a sudden invasion by organisms which had been smoldering in the middle ear and in a few of the mastoid cells for a long period of time, which had produced a septic thrombophlebitis with an invasion of the meninges or the blood stream? Does this, on the other hand, represent the acquisition of a new organism from the environment which has then invaded, very rapidly, soon after entry into the body? Many minor events, like the onset of an ordinary viral coryza, will certainly precipitate invasion by organisms that are already present in the nasopharynx. In general, if a person has carried an organism for quite a period of time, he usually has some immunity, yet at the same time the meningococcus, for example, can produce intermittent recurrent bacteremia for many months in older individuals, despite the fact that the individual has a smoldering focus. We know that the pneumococcus, at certain times, can break out from sites of infection like the middle ear, and that the staphylococcus invades repeatedly from foci of old osteomyelitis. I should think the really overwhelming character of the sepsis suggests that this is a new organism acquired at this particular time and it is probably present in the throat as the portal of invasion.

Now, why did this occur in this child? Some of the best demonstrations that the spleen has a relation to resistance were given by Lauda[1] and Mayer, Borchardt, and Kikuth[2] in their studies of Bartonella infections in rats. Rats with bartonellosis endemically have a quiescent infection, but if the spleen is removed they very quickly develop a septicemia with *Bartonella muris*. In recent years, perhaps because splenectomy has become a more popular operation, and because overwhelming sepsis is becoming rarer since it is usually snuffed out by antibiotic therapy, attention has been called to the fact that splenectomized children do seem to run a special hazard in regard to overwhelming sepsis. The first report I know anything about (but probably Dr. Farber will pull one out of the literature of thirty years ago to show me) was by Shumacker and King[3] from Indianapolis who reported, I believe, seven cases of meningococcus meningitis occurring in children who had had splenectomy for hematologic problems in general, most of them occurring in early life. I know that our group here has reviewed this problem and we have several children in whom there has been recurrent sepsis; these children had splenectomies because of thrombocytopenic purpura or hemolytic anemia when they were quite young. Dr. Diamond's group[4] found that about 15 per cent of children who have had splenectomies under the age of 2 years have had one or more bouts of rather abrupt and sudden septic infection. Dr. Carl Smith and his group[5] at New York Hospital have called attention to this phenomenon and to the frequency of

idiopathic pericarditis in this same group of children.

It is of interest that one of our patients who underwent splenectomy has had recurrent difficulty with his ears. I urged our otolaryngologist, Dr. Flake, to remove his adenoids, and then to clean out his mastoids, but even after all this was done, the boy had another bout of pneumococcal sepsis.

Several other people have told me about individual cases of this sort, so I think there can be no doubt that this is a real hazard. Each time, of course, that the medical man interferes with nature, sooner or later he turns up something that nobody thought of ahead of time. This is particularly applicable to tonsillectomy, which, although it used to be almost a routine pediatric procedure twenty years ago, is now an operation which most pediatricians do their best to avoid, for the simple reason that we know that the incidence of bulbar poliomyelitis in those few children who contract polio is much higher in the group who have had a tonsillectomy than it is in those who have not. A consequence of splenectomy in early life, then, appears definitely to be an increased chance of overwhelming sepsis in patients with severe bacterial infection.

How this happens, I think, is very difficult to know. Dr. Gitlin has made a few studies of some of these children, and there seems to be nothing wrong with their immune mechanism as judged by their capacity to form antibodies. The spleen has multiple functions, but one of its functions is the clearing of infectious agents and other foreign particles from the circulation and the formation of antibodies to them. As particulate matter in the periphery tends to pass through the regional lymph nodes by way of the lymphatics, and proteins are fed into the circulation in general by way of the lymph, so the interposition of lymph nodes performs a double function of filtering out infectious agents and then forming antibodies to them, which are then released into the efferent lymph. The spleen pretty clearly performs this same role with regard to the circulating blood. It is not the only clearing organ of the circulating blood, because the liver has Kupffer cells which do this, and the lungs and bone marrow also play some part in this whole system, yet the spleen is one of the most important of these filtering organs. The liver's clearing function is obvious, but it is related particularly to those particles which come from the gastrointestinal tract, because of the peculiarities of the portal circulation. The individual with cirrhosis of the liver very often has some difficulty with this, and brief bouts of *Bacillus coli* bacteremia are not infrequent in individuals with portal cirrhosis of the liver. By removing the spleen, we have made it harder for the individual to make antibodies to antigens that come by way of the general circulation, and in addition, we have taken away perhaps the most important filtering organ, especially designed for removal of circulating organisms. Anybody can get cataclysmic overwhelming sepsis, and otherwise perfectly normal children occasionally still die of meningococcal sepsis, and, previously, died of hemolytic streptococcal bacteremia. If we remove this organ from children very early in life, before they have developed their full degree of immunity and bacterial allergy, and all the changes which combine to make one resistant to infection,

we have deprived them of one of their major defensive organs at a time in life when bacteremia certainly occurs with infections more often than it does later on.

The only question left to be resolved here and discussed is why there was splenomegaly in the first place. One would guess that the liver is not going to be completely normal in this child. Perhaps Dr. Craig will find a reason for the portal hypertension which she seems to have had, which created this splenomegaly which led to the operation, and which then resulted in a bout of overwhelming sepsis. I think the lesson the clinician should draw from this case is that these children are similar in their need for emergency care to the children on whom Dr. Matson has performed an operation for hydrocephalus. In those cases we must tell the parent that if the child with a subarachnoid-ureteral shunt has any episode which makes it impossible for him to take fluid by mouth, he must be brought to the hospital immediately so that parenteral fluid can be supplied to replace the losses which are occurring by way of the urinary passage from the spinal fluid. Now, we have the same sort of situation here; any infection in these splenectomized children must have serious consideration, and they should be placed on antibiotic therapy the minute they get sick.

DR. CRAIG.—Do you think, Dr. Janeway, that the dental work performed the day before death may have set this thing off?

DR. JANEWAY.—It depends on what was done. I do not believe that the ordinary filling of teeth or cleaning would have any connection, but if she had extraction of teeth, then, as you know, there is almost always an invasion of the blood for about ten minutes following extraction. This has some relation to the onset of subacute bacterial endocarditis in susceptible individuals.

DR. JOHN A. V. DAVIES.—This child had some vaginal discharge. We know that occasionally beta hemolytic streptococci and other organisms are recovered from girls with leukorrhea. In the past we used to discount the whole thing on a physiological basis, but cultures frequently contain pathogens; the discharge often clears up on adequate chemotherapy.

A further possibility is that the child had a smoldering abscess in a silent area of the brain, which then ruptured into the meninges and caused a sudden widespread infection with increased pressure and retching, which has been described. Patients with overwhelming sepsis may vomit, but do not do so to this degree.

DR. R. CANNON ELEY.—I am inclined to agree with Dr. Davies that this child could easily have had meningitis, as well as an extradural abscess. I have seen such processes smolder for years and then rupture into the meninges. This child died so rapidly that one must consider that increased intracranial pressure (with the history of headache, retching, and sudden death) was the main cause of death.

DR. CRAIG.—This child, as Dr. Janeway predicted, had an overwhelming infection, a pneumococcus being recovered from the cerebrospinal fluid, heart's blood, and the lung. Numerous petechiae were present in the skin and

Fig. 1.

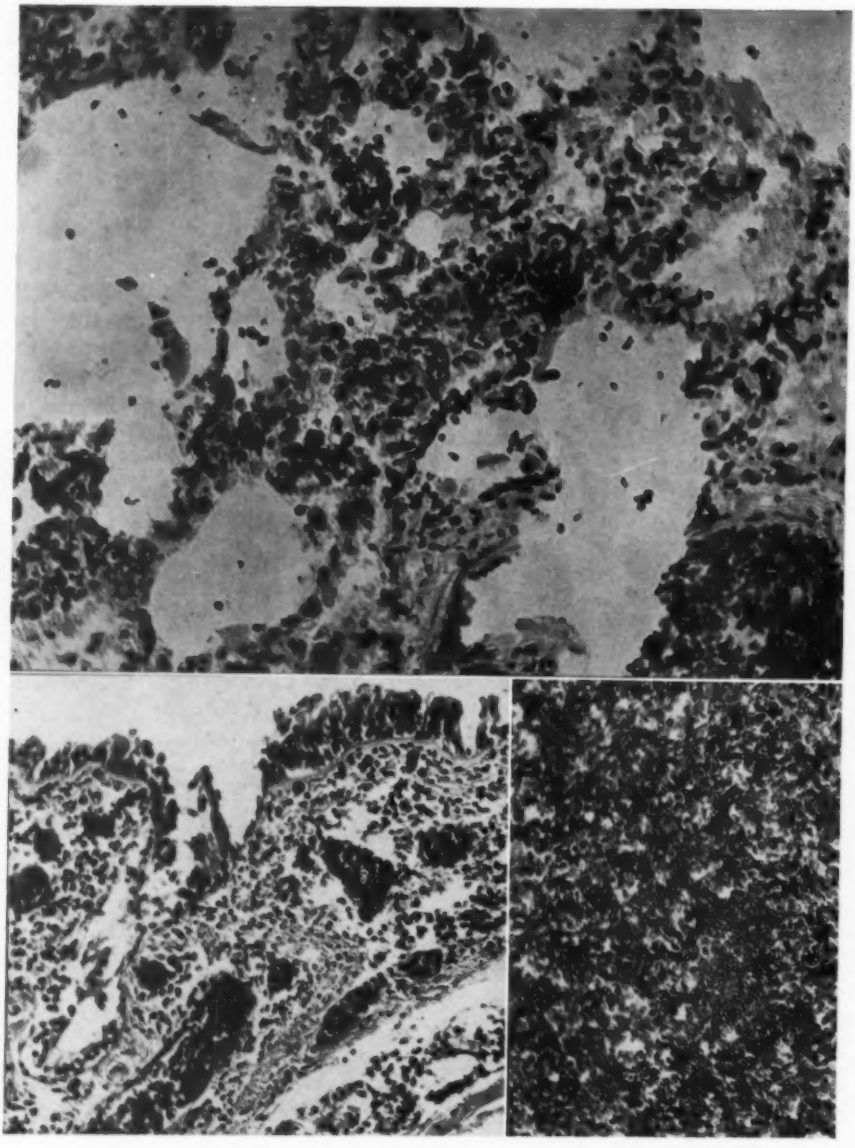


Fig. 2.

Fig. 3.

Fig. 1.—Photomicrograph, lung. Congestion of the alveolar capillaries and a minimal alveolar exudate are present (Hematoxylin and eosin; ×220.)

Fig. 2.—Photomicrograph, trachea. The mucosa and submucosa are infiltrated with leukocytes. There is congestion. (Hematoxylin and eosin; ×170.)

Fig. 3.—Photomicrograph, adrenal. The adrenal sinusoids are intensely congested but no disruptive hemorrhage is present. (Hematoxylin and eosin; ×190.)

peritoneal surfaces. There were widespread inflammatory cell collections in many viscera, in the heart, in the subendocardial areas, in the lungs (Fig. 1), in the tracheal mucosa and submucosa (Fig. 2), in the adrenal cortex (Fig. 3), and in the portal areas of the liver (Fig. 4), there were focal accumulations of inflammatory cells, in some areas being associated with parenchymal necrosis. There was no evidence of meningitis histologically, and the mastoid air cells were clear. The lymphoid tissue in the paratracheal regions had an acute reaction consistent with infection. We obtained sections of the spleen from the Children's Hospital of Philadelphia through the courtesy of Drs. Wagner and Wolman. While the splenic sections had the "inside out" arrangements of "hypersplenism" in the Malpighian follicles, and evidence of erythrophagocytosis, there was no evidence of congestive splenomegaly. The portal pressure of 200, Dr. Janeway, is within normal limits for an adult, though I have not been able to find any similar values for children.

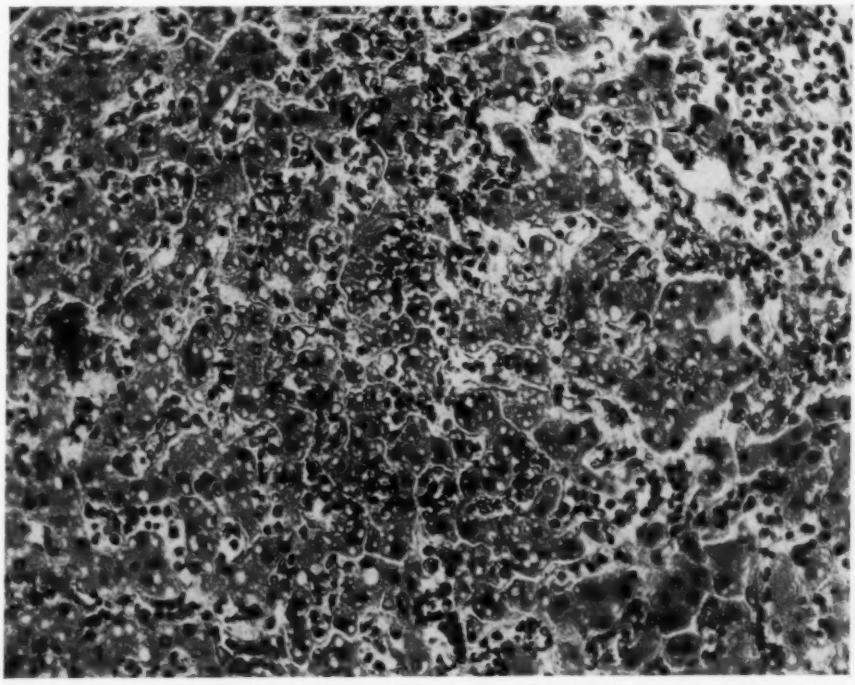


Fig. 4.—Photomicrograph, liver. The sinusoids are slightly dilated and contain an unusual number of leukocytes. In the portal triad, at the upper right, there are many lymphocytes. (Hematoxylin and eosin; ×320.)

DR. RICHARD HOEFNAGEL.—I have seen five children with this syndrome of repeated severe sepsis after splenectomy in the first year of life. Two are interesting, in that they were brothers, who differed one year in age. In July, 1951, both these children came

down, at the same time, with a hematological syndrome which was diagnosed after proper bone marrow examination and other studies, as idiopathic thrombocytopenic purpura. They were given a trial on steroids and, after an initially good response they relapsed, so that in February, 1952, on the same day, the spleens were removed from these children. They did very well after splenectomy, with no recurrence of bleeding tendency and a normal peripheral count. In September, 1952, when they seemed perfectly well, they both woke early in the morning, vomited a few times, and were apparently very ill. On the way to the hospital, both developed circulatory collapse. One died a few hours after admission to the hospital with the picture of Waterhouse-Friderichsen syndrome; he was covered with petechiae, he had no pulse, no blood pressure, and a temperature of 107° F. The other was not so ill but had a temperature of 106° F.; only after the application of vigorous therapy did he recover. The only organism recovered was a hemolytic streptococcus from the spinal fluid, which contained inflammatory cells. The child that recovered had no residual after this admission and did well until February, 1953, when, again early in the morning, after having been considered quite well, he awoke and within a few hours was in complete peripheral collapse with a fever of 106° F. No organisms were recovered. His plasma proteins were studied by Colonel Bruton and found to be entirely normal. The child, nevertheless, was put on prophylactic gamma globulin injections and the parents were given instructions to start treating vigorously any infection—even before bringing the child to the hospital. Nevertheless, a year later, with a similar clinical picture, the child was admitted to the hospital and died.

DR. CRAIG.—I think it might be interesting to summarize the experiences being published in the literature. Gofstein and Gellis[6] have gathered 107 splenectomy cases (for idiopathic thrombocytopenia, purpura, and congenital hemolytic icterus) from this institution, six of them with severe sepsis. All six of these had pneumococcus infections. King and Shumacker[3] did not give the size of the group from which their series was taken, but they had two meningococcus organisms and one *Hemophilus influenzae* organism. Smith and coworkers,[5] with forty splenectomy cases, had fourteen severe infections, six with pneumococcus, two *Bacillus coli,* one salmonella, one *H. influenzae,* and one *alpha-Streptococcus,* so that if one considers all these cases, with Dr. Hoeffnagel's cases, the pneumococcus is by far the predominant organism in the syndrome. Eleven of all were pneumococci, two meningococci, two influenzae, two coli, one salmonella, one streptococcus, and in six no organisms were cultured, although they presented a similar picture. It is of interest that the most frequent organisms here, the pneumococcus, the meningococcus, and the *H. influenzae* all have capsules of a polysaccharide nature.

DR. FRED ROSEN.—I would like to ask Dr. Janeway if he is familiar with the studies of Felton and colleagues[7] at the National Institutes of Health. Dr. Felton has induced a pseudoparalysis of the immune system by injecting pnuemococcus polysaccharides into mice. Do you think that there is any

possible relationship between this phenomenon and that which we are seeing in the splenectomized children?

DR. JANEWAY.—Dr. Gitlin has studied one or two of our patients with this sort of difficulty; they have appeared to respond to injected antigens perfectly normally.

I do not like the term "immunological paralysis" and I do not know what to call it. There is some sort of inability to form specific antibodies and it is a very specific phenomenon; you can overload the system with a particular antigen and the individual will not respond—nor will the animals—to that antigen, but they will respond quite normally to any other antigen, even quite closely related. I believe, Dr. Farber, that bacterial invasion occurs a good deal more often in young children, with their primary infections, than we realize. Under ordinary circumstances, the blood and lymph—the clearing mechanism—handle these things, giving the child time for the normal mechanisms of specific antibody formation and phagocytosis to operate. I do not believe that the agammaglobulinemic child's difficulty is so much the lack of antibody as it is the inability to form it when suddenly faced with a tremendous infection.

DR. FARBER.—I think one or two other points may be of interest.

In the days before antibiotics and antimicrobial agents, the organism which caused the fulminating picture in the young was more commonly the *Streptococcus hemolyticus*, not the pneumococcus. I was struck by the preponderance of the pnuemococcus here. The Waterhouse-Friderichsen syndrome, of course, is no longer associated merely with the meningococcus or with one organism. In this case there was hemorrhagic and actual necrosis in the adrenal, associated with a pneumococcus. The first patient that I can recall who died of infection after a splenectomy was one of two sisters with Gaucher's disease, about fifteen to twenty years ago. Their mother and their aunt had undergone splenectomies in Chicago because of Gaucher's disease, and one of the two girls, about one year after splenectomy, died of a meningococcus meningitis.

DR. CRAIG.—That patient would not be included in the series of Gofstein and Gellis. There are also other patients who had their spleens removed because of portal hypertension, one of whom, I remember, died very suddenly in 1941 of pneumococcal sepsis.

REFERENCES

1. Lauda, E.: Ueber die bei Ratten nach Entmilzung auftretenden schweren anämischen Zustände. "Perniciöse Anämie der Ratten." (Zugleich ein Beitrag zum normalen und pathologischen Blutbild der Ratte), Virchows Arch. path. Anat. **258**: 529, 1925.
2. Mayer, M., Borchardt, W., and Kikuth, W.: Ueber Einschlüsse der Erythrozyten bei experimentaller Anämie der Ratten, Klin. Wchnschr. **5**: 559, 1926.
3. King, H., and Shumacker, H. B., Jr.: Splenic Studies. I. Susceptibility to Infection After Splenectomy Performed in Infancy, Ann. Surg. **136**: 239, 1952.
4. Diamond, L. K.: Personal communication.
5. Smith, C. H., Erlandson, M., Shulman, I., and Stern G.: Hazard of Severe Infections in Splenectomized Children, A. M. A. J. Dis. Child. **92**: 507, 1956.
6. Gofstein, R., and Gellis, S.: Splenectomy in Infancy and Childhood. The Question of Overwhelming Infection Following Operation, A. M. A. J. Dis. Child. **91**: 566, 1956.
7. Felton, L. D., Kauffmann, G., Prescott, B., and Ottinger, B.: Studies on the mechanism of the Immunological Paralysis Induced in Mice by Pneumococcal Polysaccharides, J. Immunol. **74**: 17, 1955.

Medical Progress

HYALINE MEMBRANE DISEASE

PAUL CURTIS, M.D.*
NEW YORK, N. Y.

THE pulmonary hyaline membrane is a frequent pathological finding in neonatal autopsies on liveborn children. The first description of the lesion appeared in 1903, but it was not until 1946 that it became a frequent topic in the pediatric literature.[1] Landing[2] reports it as one of the more common findings in neonatal autopsies and by inference seems to imply that the hyaline membrane is associated with the leading causal factors in neonatal death. The hyaline membrane disease, however, is not a recognized clinical entity and there is no mention of it in the manual, *Standard Nomenclature of Disease*. There is marked disagreement as to its chemical and physical nature, little knowledge of the mode or modes of its production, and no understanding of its treatment.

PATHOLOGICAL DESCRIPTION

Potter[3] describes the advanced disease picture as follows: "The lungs in hyaline membrane disease are the size of well expanded lungs, but have the consisteney of liver. They are a uniform dark red purple in color and sink in water. Histologically there is widespread reabsorption of air and the walls of many alveolar ducts and most alveoli are collapsed giving a solid appearance to the lung parenchyma between the few alveoli that remain open. If an attempt is made to expand such lungs with air after removal from the body, the proximal spaces become greatly hyperdistended and the distal ones even more collapsed. If fluid is injected however, the lung spaces gradually open. An intense capillary engorgement is present and is responsible for the gross color and increase in weight. If the infant has survived more than 48 hours, an inflammatory process is superimposed. The inner surfaces of the alveolar ducts that remain open are covered by an irregular layer of homogeneous acidophilic material."

This material, the hyaline membrane, is thought to serve as a mechanical barrier to normal respiratory exchange by blocking off some portions of pulmonary tissue and by coating the remainder so that capillaries are deprived of contact with the oxygen-carrying atmosphere. Behrle has shown that prematurity per se and hyaline membrane are factors interfering with lung expansion.[4] Blood, edema fluid, or purulent exudate do not interfere with lung expansion. Specific morphologic and histochemical details will

*Address: 545 East 14th Street.

be considered in the discussion of the theories of etiology of the hyaline membrane.

During 1948-1951, several reports appeared in the literature by Kaufman[5] and by MacMahon,[6] describing a condition they termed "congenital alveolar dysplasia of the lungs." This was described as defective and hypoplastic development of the alveoli with excessive interstitial tissue resembling fetal mesenchyme and devoid of mature collagen fibrils. Though these articles make no mention of any hyaline material, later authors have claimed that alveolar dysplasia is really a variant of the hyaline membrane picture.

Recent authors have depreciated the role of the hyaline membrane itself and emphasized the importance of atelectasis of the alveoli as the chief pathology.[7] Landing notes that the presence of hyaline membrane seems to correlate with an absence of other lethal factors such as severe congenital heart disease.[8] Smith[9] considers pneumonitis and pulmonary hemorrhage to be unrelated findings since they are seen with equal incidence both with and without hyaline membrane disease.

Potter[3] reports that the only associated finding is a tendency to an increase in the subarachnoid fluid. The normal amount of fluid varies with age. The premature infant weighing 1,500 to 2,000 grams has more fluid actually and proportionally than infants of any other weight. The normal amount at this weight is 10 to 15 c.c., but in infants with hyaline membrane delivered at term by cesarean section, 40 to 60 c.c. of fluid may be obtained.

OCCURRENCE

The largest clinical survey of what at post-mortem examination proved to be hyaline membrane disease is reported from Johns Hopkins Hospital.[10] Between 1937 and 1949, 30.5 per cent of the liveborn infants who came to autopsy had some degree of hyaline membrane disease. The grouping by weight is of interest.

As in other reported series, no hyaline membrane was detected in any stillborn infants. The author calculates a "hyaline membrane rate" of 3.7 per 1,000 liveborn infants weighing between 1,000 and 2,499 grams and an incidence of 0.99 in full-term infants.

Landing[2] reports that 85 per cent of unselected autopsies on newborn infants show lung lesions and that 45 per cent of these are aspirated amniotic sac contents. This group in Landing's series consists largely of hyaline membrane cases. In the Johns Hopkins review,[10] as in other reported series, no cases were seen in infants surviving less than 1 hour or more than 3 days. These authors note an inverse proportion between the length of life and the extent of membrane formation; infants surviving longest had less extensive membranes than

INFANTS GROUPED BY WEIGHT (GRAMS)	PER CENT WITH HYALINE MEMBRANE DISEASE POST MORTEM
2,500 plus	17
2,000-2,499	47
1,500-1,999	38
1,000-1,499	33
400- 999	25
Total premature infants	38

those dying quickly and had a higher incidence of associated pneumonitis.

RELATION OF PREGNANCY AND DELIVERY COMPLICATIONS TO HYALINE MEMBRANE DISEASE

Many authors have attempted to correlate complications of pregnancy and delivery to hyaline membrane disease. The generally accepted ones seem to be prematurity, cesarean section, maternal diabetes, fetal distress, and placenta previa. The Hopkins group,[10] after a review of several articles and the statistics of their own series, presented the following figures:

COMPLICATION OF PREGNANCY	NUMBER OF TIMES MORE THAN EXPECTED INCIDENCE THAT HYALINE MEMBRANE WAS FOUND
Maternal diabetes	18
Cesarean section	8
Prematurity	7
Breech delivery	6
Multiple pregnancy	4
Maternal toxemia	3

(Probably there is some overlap in these figures, since twins tend to be born prematurely, labor may be induced in toxemic patients, etc.)

CLINICAL PICTURE

There is no clear-cut information on how the syndrome of hyaline membrane presents. Traditionally, the infant is said to be healthy at birth, but in reviewing the autopsy cases in which hyaline membrane and no other known cause of death could be ascertained, Latham[10] breaks down the group as follows:

CONDITION AT BIRTH	PER CENT
Excellent	26
Fair, poor respiration, good heart	36
Poor, apneic, fair heart	31
Poor, apneic, irregular heart	5
Poor, fair respiration, poor heart	2

A series from Kings County Hospital[11] reports a significant increase in ante-partum hemorrhage and notes that 42 per cent of the mothers were admitted to the hospital for some complication of pregnancy. Only 10 per cent of the infants were in good condition when they arrived in the nursery. In 5 twin gestations terminating prematurely in this series, only one case showed hyaline membrane in both twins. In the remaining pairs, hyaline membrane was always seen in the twin delivered first. Gilmer[12] reports that there is rarely a period of normalcy during the life span of a child found to have extensive hyaline membrane disease at autopsy.

Theoretically, the clinical course of hyaline membrane disease is one of increasing dyspnea, cyanosis, retractions, and finally death in anoxia. Haddad[13] reports that respiratory rate alone is a good index of the progress of the disease. Apgar has devised a more complex scoring system in which values are assigned for the presence or absence of chin movement, expiratory grunt, xiphoid and intercostal retraction and the synchronization of abdomen and chest movements.[14] These theories may be of some value as clinical guides, but Blystad[15] has described a group of children who, rather than showing dyspnea, simply slowed down and stopped breathing as the clinical manifestation of hyaline membrane disease.

ROENTGEN DIAGNOSIS

X-ray studies in hyaline membrane are rather confusing. Caffey[16] claims that lung expansion at birth may take several days with areas of atelectasis which gradually clear being evident in

lungs of clinically normal children who stay normal. Donald[17] reports that he can identify hyaline membrane disease roentgenographically with no false negatives and rare false positives by finding fine miliary mottling throughout the lung. This marking becomes progressively coarser and more coalescent and may finally become confluent in fatal cases. Petersen[18] claims that the normal neonatal lung shows normal lung fields with evidence of full expansion within 15 minutes after birth. He describes the x-ray picture of hyaline membrane disease as a finely reticulogranular pattern with general increase in lung density, appearing uniform throughout the lungs. He differentiates this from the picture of fetal aspiration in the postmature infant, which is said to show a coarse irregular pattern, nonuniform with focal irregularities in aeration.

PHYSIOLOGIC CHANGES

The changes which occur in pulmonary and circulatory physiology in hyaline membrane disease are now coming under investigation. Before discussing these data, it is of interest to note that the normal newborn infant differs from the older infant and adult in response to respiratory stimuli.

The minute volume of the healthy newborn infant diminishes when exposed to low oxygen. After a few days of extrauterine life, both term and premature infants respond to hypoxia by a marked increase followed by a slight fall in minute volume.[19, 20] All infants at birth show an acidosis correlating with high plasma levels of lactic and pyruvic acid.[21] During the first hours after birth pH rises from 7.33 to 7.43 with no change in plasma CO_2 content. There is some fall in CO_2 tension and some rise in O_2 tension. After the first few hours of life 5 per cent CO_2 is a more powerful respiratory stimulant than 100 per cent oxygen and causes a quicker restoration of minute volume to infants hypoventilating after anoxia. In fatal cases of hyaline membrane disease Blystad[22] notes increased CO_2 tension, accentuation of metabolic acidosis, decreased values for pH, and low oxygen tension.

Plethysmographic studies of lung volumetric measurement in the newborn infant are difficult because it is hard to maintain the baby in a steady state during an experimental run. It is difficult to get an infant to relax in an apparatus with a small dead space. Howard[23] concluded that neonatal respiration presents multiple patterns, that respiratory rate and tidal air have a wide range. He could find no constant values for even as short a period as 10 seconds. Smith, Cook,

INFANT	MIN. VOL.	RATE	TIDAL VOL.	CRYING VITAL CAP.	ALVEOLAR VENTILAT.
Normal	498 ml.	34	15 c.c.	140 c.c.	355 ml./min.
With respiratory distress	+75%	+90%	Normal	−50%	−30%

	ARTERIAL CO_2 TENSION	FUNCTIONAL DEAD SPACE	FUNCTIONAL RESIDUAL CAPACITY	NEG. PRESS CHANGE IN RESPIRATION	MAXIMUM PRESSURE CHANGE
Normal	32 mm. Hg	5 ml.	70 ml.	5 cm. H_2O	50 cm. H_2O
With respiratory distress	+30%	+70%	−45%	+300%	?

	LUNG COMPLIANCE	PUL. WORK/MIN.
Normal	5 ml./cm. H_2O	1,450 gram. cm.
With respiratory distress	−80%	+400%

Sutherland, Lucey, Drorbaugh and others[24-26] have tentatively established the following values for the 2.5 kilogram infant during the first week of life.

The functional dead space change may be due to abnormal gas distribution in the lung, disturbance in diffusion across respiratory epithelium, or vascular changes like failure of perfusion of an alveolar area with blood.

Lung compliance is the volume response of lung per unit of pressure applied (Hooke's law). It is the ratio of tidal volume to intrapleural pressure (measured as intraesophageal pressure) at instants of no flow. The investigators report that lung compliance was the single best index of the degree of pulmonary pathology. Expressed in milliliters of air per centimeter of water per kilogram, the value for the normal term newborn infant at birth is 1.3. In the normal child this falls within a few minutes as the lungs expand to a value of 1.1.

Minute volume—tidal volume × frequency.
Tidal volume—volume inspired in each cycle.
Vital capacity—maximum amount that can be expelled from lungs following maximum inspiration.
Alveolar ventilation—tidal volume—dead space (air in dead space has same composition as that in the alveoli left over from the last breath)
Functional dead space—anatomical dead space + volume of gas ventilating alveoli that have no capillary flow + volume of gas ventilating some alveoli in excess of that required to arterialize the pulmonary capillary blood flowing around them.
Functional residual capacity—disadvantageous when small, for alveolar pO_2 fluctuates widely throughout respiratory cycle—coming close to venous pO_2 during expiration and to inspired pO_2 during inspiration. This leads to uneven ventilation and tends toward anoxemia.

ETIOLOGY

The histochemical, physiological, and experimental approaches to hyaline membrane disease can be divided into three main theories. These are (1) aspiration of amnionic or gastric contents, (2) transudation on the basis of some special type of heart failure thought possible only in the neonatal cardiovascular setup, and (3) exudation due to toxic external influences like oxygen poisoning.

The aspiration theory: Snyder has demonstrated that respiratory-like movements of the fetus occur at least fairly frequently in many animals including man.[27, 28] Potter has shown that the human fetus swallows and "breathes" Thorotrast containing amniotic fluid.[27] These experiments were done in early pregnancies in which the mothers were candidates for therapeutic abortion. In fetuses nearer term, proof of respiration by x-ray demonstration of Thorotrast in the fetal lungs was possible in only a few of the cases. In both animal and human experiments of this type there is evidence of foreign material in the lung apparently due to absorption of the amniotic fluid in the lung.

Hypoxia or anoxia in the fetus in many animal species causes exaggerated respiratory movements in the fetus in midpregnancy but does not produce these in fetuses near term.[29] However, in fetal sheep it has been

shown that certain activities may be normally inhibited by certain nervous system centers. Anoxia can be shown to depress these centers if it is of sufficient degree and may allow the release of activity. Progessive anoxia will in time suppress all activity.

Farber[30] considered the hyaline membrane to be fused, resolving exudate consisting of necrotic mononuclear cells, leukocytes, red cells, altered fibrin, or aspirated amniotic sac contents. He compared the infant hyaline membrane with a membrane seen in influenza pneumonia in adults. The location of the membrane was thought to represent mechanical dispersion of foreign material toward the periphery of the air sacs by violently inspired air. He showed that horse serum, India ink, or fibrinopurulent exudate instilled into the trachea of various experimental animals would assume the distribution of the classical hyaline membrane if the animals were subject to vigorous artificial respiration in the Drinker respirator.

Claireaux[31] notes that special stains of the hyaline membrane indicate the presence of fat and polysaccharides. Cells can be seen in areas of hyaline membrane that are still organizing and these are identifiable as flat squames from the liquor amnii. Samples of centrifuged amnionic fluid sediment resuspended in saline and incubated at 37° C. lose cellular outlines and become eosinophilic. If this material is inoculated into the trachea of a live rat, the picture in the drowned lung resembles hyaline membrane. Absorption of large volumes of water by the fetal lung would also create a concentrated amnionic sediment.

Landing emphasizes that two factors are necessary—a large amount of amnionic fluid to provide the necessary particulate matter and a definite period of air breathing to mechanically compress the material against the walls of the lung passages.[27] Landing has shown that the squamous cell count in amnionic fluid rises in the latter months of pregnancy. He correlates this with an increased incidence of squames incorporated in the hyaline membranes seen in infants born near term.

Negative evidence is provided by Lelong,[32] who, along with other authors,[2, 27] notes that in certain cases of obvious massive amnionic aspiration with accumulation of cornified cells in many air cavities no hyaline membrane is formed in spite of survival of several hours to days. In the only human experiment reported, Potter was unable to demonstrate hyaline membrane in the lungs of an anencephalic monster who died several hours after the introduction of 80 c.c. of amnionic fluid via tracheal catheter.[27]

Ahvenainen refines the aspiration theory by suggesting the role of aspiration of vomited amnionic fluid.[9] He notes that there is occasional desquamation of bronchial epithelium and emphasizes the role of acid gastric juice in hyaline membrane formation. Gellis and other authors[33, 34] have observed that the stomachs of infants born by cesarean section, especially those of diabetic mothers, contain excessive amounts of fluid, and feel that routine aspiration of the stomach at delivery has reduced the incidence of respiratory complications in their nurseries.

The most complicated theories of hyaline membrane formation may be grouped under the heading of transudation or exudation. The simplest

scheme is advanced by Reuther,[35] who feels that anoxia is the etiologic factor in hyaline membrane disease. He feels that this causes increased capillary permeability with exudation into the alveoli from the vascular alveolar walls.[36] This liquid material is then pressed against the alveoli by respiratory movements.

Indirect evidence for a vascular component contributing to hyaline membrane is found in certain diseases in which an apparently classical hyaline membrane is produced in the lungs[1, 37, 38]; chicken pox, poliomyelitis, sulfonamide hypersensitivity, subacute bacterial endocarditis, metastatic carcinoma of the lung, Hodgkin's disease, uremia, milk aspiration, radiation pneumonitis, influenza pneumonia, rheumatic pneumonia, war gas pneumonitis, and plague. The hyaline membranes seen in these conditions have been described as the result of vascular damage with increased capillary permeability. Further evidence to support the role of the vascular tree in the production of hyaline membrane is offered by Gilmer, who describes the appearance of hyaline membrane beneath and endothelial basement membrane when it is present in small quantities.[10] When hyaline membrane is more pronounced, he reports that it disrupts the respiratory membrane and then may be found free in the alveoli mixed with squamous cells. Some authors deny the existence of a respiratory basement membrane but electron microscope studies seem to confirm its presence.

The most impressive evidence for an endogenous source of the hyaline membrane is provided by authors who describe histochemical techniques. Arwaka,[39] using isotopically labeled I^{131} attached to blood alpha globulins in guinea pigs, showed that the hyaline membrane produced by oxygen poisoning involves localized increased capillary permeability. Duran-Jorda[40] identifies hyaline membranes' chief component by ultraviolet spectrography as a member of the cytochrome group. He links it with blood-derived protein and pigment and compares it chemically to eosinophilic material found in thrombi, glomerulus precipitate, and pulmonary edema. Hadders[41] produced hyaline membrane in rats by tracheal injection of rabbit serum. He also succeeded in producing hyaline membrane by promoting the passage of blood plasma from the lung capillaries by intrathoracic injection of vasodilator substances. He used Cardophyllin, Euphyllin, and histamine successfully. Hadders suggests that the sudden increase in perfusion of lung tissue by the change in circulation at birth could cause filtration of the plasma from blood into air spaces. Possibly then, some degree of hyaline membrane formation is a normal occurrence.

Gitlin,[42] using a fluorescent antibody, identifies the main component of hyaline membrane as contracted masses of fibrin. He showed that newborn infants with other illnesses do not have significant amounts of fibrin in the lung and that there is not enough fibrin in concentrated amniotic fluid to account for hyaline membrane. He postulates an alveolar effusion as the probable beginning of hyaline membrane formation and notes that the deposition of fibrin from this effusion would be enhanced by the presence of aspirated amniotic fluid since this contains thromboplastic material.

Fresh amniotic fluid cuts the clotting time of plasma in half in the presence of calcium.[43, 44]

Further evidence for the dual origin of hyaline membrane is presented by Stevenson and Laufe.[45] They used a combination of amniotic fluid and plasma injected into the tracheas of live guinea pigs and succeeded for the first time in all the experiments of hyaline membrane production in getting the full triad of hyaline membrane, atelectasis, and engorgement. They suggest that the sequence of events is as follows: (1) the newborn infant aspirates amniotic fluid; (2) the lungs exude a high protein fluid as a result of vagal injury, irritation from amniotic fluid, high oxygen tension, anoxia, or other cause; (3) amniotic fluid clots the exudate and, as fluid is absorbed, a membrane is formed; (4) clotted exudate plugs produce atelectasis as resorption of trapped air occurs; (5) anoxia increases and the infant asphyxiates unless the changes are minimal and phagocytes can destroy the membrane and reverse the picture.

Miller and Behrle[46] produced hyaline membrane in rabbits by bilateral vagotomy, but were unable to assign a specific mechanism. They noted that brain damage can produce pulmonary edema both clinically and experimentally. Suggested mechanisms included aspiration of gastric contents and asphyxia through flabbiness of the glottis or by approximation of the vocal cords. In later investigations these authors[47] noted that phrenic nerve stimulation in the newborn failed to inhibit spontaneous respiration as it does in the adult. Sectioning of the vagus in adult dogs causes this reflex to disappear. Activity of the intercostal muscles and diaphragm are affected by vagal stimulation via the Hering Breuer reflex. Vagotomized animals show diminished and irregular activity of the diaphragm. In pneumatographic studies on infants who were later proved to have hyaline membrane these investigators felt that chest retractions were due to exaggerated expansion of the chest in an attempt to compensate for poor diaphragm function. They do not, however, offer any mechanism to tie up vagal deficiency with hyaline membrane disease.

Lynch[48] notes that in his experimental studies pulmonary edema invariably preceded hyaline membrane formation. Farber[30] explained vagotomy induced pulmonary edema as a release of strong tonic vasoconstrictor effects causing capillary dilatation, blood stasis and edema. Vagal stimulation influences the rate of pulmonary edema formation in massive saline infusions in experimental animals. Drinker[49] states that lung capillaries are physiologically different from those elsewhere in the body and cites the rapid production of pulmonary edema by two methods: the systemic injection of alpha naphthyl thiourea, and the introduction of fibrin forming mixtures, whole blood or particulate matter like India ink into the cisterna magna.

THE ROLE OF HEART FAILURE IN HYALINE MEMBRANE DISEASE

The first discussion in the literature on the significance of heart failure in hyaline membrane disease denies any causal relationship. Gellis[50] found no sign of enlarging liver, edema, venous distention, and in 60 per cent of his series no significant cardiomegaly by

x-ray or post-mortem examination. Infants of diabetic mothers, a group prone to hyaline membrane disease, are often edematous at birth.

Lendrum[51] suggests a rather elaborate heart failure etiology. He notes that the capillary bed in the fetal lung has a very limited capacity and postulates that a rise in pressure due to increased volume flow in the lesser circuit causes filtration of the blood serum from the alveolar walls into the alveolar air spaces. He assumes that this liquid barrier to oxygenation in the lungs contributes to some degree of cardiac decompensation and suggests that the left heart fails first because of its greater work load. This in turn might lead to re-establishment of right to left flow through the ductus and foramen ovale with a revision of the circulation to a fetal pattern and some bypassing of the lungs. As capillary pressure in the lung drops, edema fluid is reabsorbed and the protein component is concentrated. This theory has been criticized by Polacek[52] who notes that there is no evidence of left heart burden at birth and remarks that the oxygenation of both ventricle muscle masses depends on a common origin of coronary circulation.

Lynch[48, 53, 54] evolved the theory that uncontrolled unmodified sympathetic stimulation released by the abolition of afferent vagal chemoreceptors from the lungs is responsible for a pulmonary edema picture culminating in hyaline membrane disease. In a series of papers he describes the isolation from hyaline membrane of a metalloporphyrin which appears to be hemoglobin. In the experimental production of hyaline membrane in guinea pigs and rabbits using high oxygen tensions and bilateral vagotomy, he notes that a common sequence occurs. There is a fall in pH and CO_2 combining power, a rise in plasma potassium, serum calcium and serum inorganic phosphate. These are compatible with the development of a respiratory acidosis. Electrocardiograms taken on oxygen poisoned rabbits show left ventricle preponderance. Lynch speculates on a special type of heart failure involving only the left heart. He suggests the possibility of a fall in heart muscle potassium beyond a level at which the myofibril can relax. He reports prevention of oxygen-induced hyaline membrane in a single animal by intraperitoneal injection of potassium chloride and calcium gluconate. For his mechanism Lynch suggests that pulmonary vasodilatation in the capillary bed allows red cells to pass into the alveoli where they are lysed by diminished osmotic resistance and the physical agitation produced by respiratory motion.

Further exploration of the mechanics of the neonatal circulation should prove rewarding in hyaline membrane disease studies. Potter[55] has shown that the pulmonary vascular bed of the premature is often not capable of containing the full volume of fluid presented to it. Yloppo[9] has documented the increased vascular permeability of the premature capillary circulation. Several authors[56, 57, 58, 59] feel that pressures in the lesser circuit may be as great or greater than those in the systemic circuit at birth. Eldridge[60] gives oxygen saturation studies in normal newborns in which he shows that a majority of infants in the immediate neonatal period show a veno-arterial shunt through the ductus when challenged by hypoxia. Lind[57] emphasizes a normal neonatal circulation

for several hours in the sheep in which there is reversal of flow through the ductus so that the left ventricle contributes to the pulmonary flow. In selected newborns with catheterization-proved patent fetal circulatory channels, hypoxia can be shown to produce a precipitous fall in oxygen saturation. In some cases there is a fall in mean arterial blood pressure to a level below that of mean pulmonary artery pressure. In such cases arteriovenous shunting is established via the patent ductus arteriosus.[61] How these factors may tie in with hyaline membrane disease is not known, but certainly there is a setup in which drastic pressure and volume changes may be reversibly set up in the pulmonary blood supply.[62]

Vascular pressure and volume changes may also be invoked to explain the picture of atelectasis characteristic of hyaline membrane. Jukka[63] after doing perfusion experiments on atelectatic lungs decided that pulmonary parenchyma was to some degree an erectile tissue. Capillary filling of his excised lung specimens caused partial alveolar expansion when the bronchi were in contact with air. Cook[64] has data showing that vascular distention does produce some decrease in pressure required to maintain a given lung volume in adult dogs. He feels that in view of the large initial pressure necessary to overcome surface tension forces within the lungs in newborn animals and humans the apparently small effect of vascular distention cannot be very important.

Dr. Sutherland[65] has been kind enough to permit the inclusion of some as yet unpublished information from the Boston Lying-In Hospital.

(1) Plethysmograph studies indicate that in hyaline membrane disease states there is a shift of fluid into tissue spaces which may possibly indicate systemic manifestations of congestive failure. This change of fluid volume is reversed as the child begins to improve clinically.

(2) Urine output seems greater in hyaline membrane disease than that seen in the normal premature infant of the same weight. Urine excretion of solutes also seems greater. These factors are not seen as a diuretic phase and do not correlate in time with clinical improvement. Thus they cannot be associated with recovery from congestive failure but seem to suggest a different body composition at birth from that of normal infants.

TOXIC AGENTS AND HYALINE MEMBRANE FORMATION

Wagner[66] considers hyaline membrane derived from endogenous mucus of the nasopharynx, buccal cavity and bronchial tree. Lynch[54] before concluding that hemoglobin was the major constituent of hyaline membrane, suggested that the metallic complex present in the protein fraction of hyaline membrane might be a part of a respiratory enzyme secreted by the epithelium of the finer bronchioles in the presence of air.

Miller[67] interpreted sections of hyaline membrane containing lungs as showing denuded epithelium under areas of most massive hyaline membrane formation. He felt that the hyaline membrane might be the end result of injuries occurring in fetal life to the epithelium of the terminal air spaces.

Hyaline membrane has been successfully produced in experimental animals by x-ray, high oxygen tensions or a combination of high oxygen and high CO_2 partial pressures.[68] When any species of animal is put in oxygen at pressures ranging from 0.8 to 2 atmospheres, dyspnea, cyanosis and eventually death occur. It seems that oxygen is less irritating to the pulmonary system in man than in any other species. In the rabbit lung congestion, edema, epithelial degeneration and desquamation, fibrin formation, pneumonia and hyaline membranes are found. There is a decrease in the diameter of blood vessels in the brain and eye (no other vascular sites have apparently been studied). There is an increase in the circulating histamine. It is thought that the toxic action of oxygen at high pressures is due to its inhibitory action on certain enzyme systems. Postulated mechanisms for this include oxidation of a metallohemochromogen to an inactivated oxidized form or the oxidation of a coenzyme to an inactive form.

Szewczyk[69] in a discussion of retrolental fibroplasia predicts that vasodilatation, edema, neovascularization and transudation from blood vessels may take place in any anoxic fetal tissue which utilizes oxygen at a rapid rate. Several authors note the apparent rise in hyaline membrane disease occurs at the same time as the numerical increase in retrolental fibroplasia was noted.[36] Respiratory distress however is not a characteristic feature in reports of infants developing retrolental fibroplasia. Another objection to the idea of oxygen as an ideological agent in hyaline membrane disease is the fact that the longer the infant with respiratory distress lives in high oxygen in his incubator the less likely he is to die with hyaline membrane disease. Tran Dinh De[70] has been able to consistently produce the classical hyaline membrane with engorgement, hyaline membrane and atelectasis by using newborn guinea pigs and rats rather than the adult animals employed by previous investigators.

THERAPY

The treatment of hyaline membrane disease is poorly understood. There are few statistical studies and there seems to be no specific therapeutic agent.

A few prophylactic measures have general acceptance. Cesarean section should be avoided, and from the hyaline membrane prevention point of view it would seem wise to avoid early delivery even in the face of complications of pregnancy. In the selected group of newborns who are statistically prone to hyaline membrane disease certain prophylactic measures seem indicated even in the well appearing child. Polacek[52] advises early clamping of the cord without stripping to prevent overloading of the circulation. Several authors[33, 34] advocate routine catheter drainage of the stomachs of all cesarean babies and claim a significant reduction in respiratory distress incidence in these children. Chapple[27] notes that premature infants are born at a time when maternal progesterone levels are still high and suggests that here the hormone is responsible for fluid accumulation.

The prophylactic use of detergent mist has been advocated by many authors but recent statistical studies[71] in the use of Alevaire as against plain water vapor showed no difference in

the eventual outcome of the two groups studied. Later tests[14, 72] seem to indicate that water vapor has little or no advantage over incubator air. There seems to be general agreement that oxygen is indicated only for the appearance of cyanosis or respiratory distress.[73, 74] It would seem wise to withhold feedings on all infants who are possible candidates for hyaline membrane disease to prevent aspiration if respiratory distress develops. There are no studies reported on the routine digitalization of infants who are prone to hyaline membrane disease.

There is disagreement on the position that potential hyaline membrane babies should be kept in. The members of the aspiration etiology school advise postural drainage in the head low position.[27] The heart failure etiology group advise an erect position to minimize venous pooling in the thorax. It seems to be fairly common practice to administer routine antibiotics to the group of infants who are potential hyaline membrane candidates. This is done usually because of prematurity or complications of delivery and no one appears to advocate it as prophylaxis against hyaline membrane.

Once the actual disease is manifest clinically there are certain procedures that may be tried. There is agreement that oxygen is indicated in this condition. Smith[26] notes that high concentrations of atmospheric oxygen increase the already elevated minute volume of infants in respiratory distress by increasing the tidal volume. It is interesting to note that in normal infants Cheyne-Stokes-like respiratory irregularity disappears during respiratory distress and the breathing pattern becomes deep and regular as long as the infant is not moribund.[75]

Laufe,[43] an adherent of the transudation viewpoint, suggests nebulized intrapulmonary anticoagulants and aerosol enzymes as treatment. Gitlin[76] reports that activated plasminogen or plasmin will partially remove hyaline membranes from fresh-frozen dried and mounted sections of lung. Distention of such fresh lungs with plasmin in saline or buffer at a limit of up to 380 units per c.c. will not significantly remove the membranes after 1-12 hour incubation periods.

In guinea pig hyaline membrane produced by oxygen poisoning, Bruns[77] showed that aerosols of hyaluronidase and trypsin only served to enhance hyaline membrane formation. Humidifying the oxygen did not influence the rate or incidence of hyaline membrane formation, but Alevaire and an aerosol of ethyl alcohol markedly decreased the amount of hyaline membrane produced. If animals of either sex were given progesterone or chorionic gonadotropin and then exposed to high oxygen they died more rapidly with hyaline membrane and "showed more pulmonary vascular disruption" than any other group. ACTH administration seems to increase the amount of hyaline membrane formation in oxygen poisoned guinea pigs. Cortisone[13] has no effect on the incidence of hyaline membrane disease seen in infants of diabetic mothers. Pilocarpine enhances the production of experimental hyaline membrane but no one has tested the effect of vaguslike drugs on the animal or human disease.[48]

Physical exhaustion and tolerance of the central nervous system are probably the critical factors in neonatal resistance to anoxia. A number of investigators have considered temperature control as a means of tiding an

infant over the coarse of his disease. It is known that the speed of chemical reactions important to life is doubled or tripled with each 10 degree rise in temperature. Miller[79] has shown that the life of the newborn rat in conditions of absolute anoxia is prolonged threefold if the animals are chilled 10 degrees. It has been suggested that hypothermia be applied to hyaline membrane disease patients whose respiratory rates rise over 100 per minute.[25] In a recent study on the influence of thermal environment upon the survival of premature infants in the first five days of life however, a significantly higher survival rate was observed in the "normothermic" group.[79]

Carbohydrates are the most important anaerobic source of energy in the newborn. Hyperglycemia produced by subcutaneous glucose water injections markedly increases the ability of newborn rats to survive anoxia. Conversely insulin induced hypoglycemia or poisoning of the glycolysis cycle with iodoacetate or fluoride decreases survival time in anoxic newborn rats.[80]

Fifty-five newborn infants of diabetic and "prediabetic" mothers who exhibited respiratory distress are reported on by Reardon.[81] Severe respiratory distress was present at birth in infants who subsequently developed symptoms of respiratory distress. Metabolic acidosis appears several hours later in all infants. Blood glucose concentration was shown to be significantly decreased at 2 to 4 hours of age. Infants treated with 30 ml. per pound per day of 5 per cent glucose and 0.45 Gm. per cent saline by mouth or parenterally showed marked clinical improvement and a return of arterial pCO_2 to normal within 24 hours. The difference in death rate associated with hyaline membrane in this group and in an untreated control group was statistically significant.[81]

Miller[4] in post-mortem studies felt that intermittent positive pressure breathing would not be of value in hyaline membrane disease. Goddard[82] shows autopsy pictures of lungs with hyaline membrane and collapse in which alveolar dilatation was produced by 40 cm. of pressure and the hyaline membrane fragmented so that, according to the author, a space is created for respiratory exchange. No clinical trials are reported.

Day[83] describes the use of an electrophrenic respirator as an aid in management of what he calls secondary atelectasis. His studies would seem to indicate that this form of treatment is of little value in cases of pure hyaline membrane disease.

Preservation of the chest contour is advocated by several authors to improve respiratory mechanics. Love[84] uses a rubber band supported towel clip to prevent retraction of the sternum and feels that the mechanical advantage of the thoracic cage is increased by this procedure. Townsend[85] advocates stiffening the thoracic cage with adhesive tape and splints to prevent retraction and thus oppose intrapleural negative pressure. He has successfully treated atelectasis in older children in this way and suggests the application of the method to treating hyaline membrane disease.

SUMMARY

A review of the literature relating to the possible causes, composition, and treatment of "hyaline membrane disease" has been presented.

REFERENCES

1. Tran Dinh De: Hyaline-like Membrane Associated With Diseases of the Newborn Lungs, Obst. & Gynec. Surv. **8**: 1, 1953.
2. Landing, B.: Pathologic Features of the Respiratory Distress Syndrome in Newborn Infants, Am. J. Roentgenol. **74**: 796, 1955.
3. Potter, E.: Pathology of the Fetus, Chicago, 1952, Year Book Publishers, Inc.
4. Behrle, F. C., Gibson, D. M., and Miller, H. C.: The Role of Hyaline Membranes, Blood, Exudate, Edema Fluid and Amniotic Sac Contents in Preventing the Expansion of the Lungs of Newborn Infants, Pediatrics **7**: 782, 1951.
5. Kaufman, N., and Spiro, R. K.: Congenital Alveolar Dysplasia of the Lungs, A. M. A. Arch. Path. **51**: 434, 1951.
6. MacMahon, H. E.: Congenital Alveolar Dysplasia of the Lungs, Am. J. Path. **24**: 919, 1948.
7. Dawson, J. R.: The Pathogenesis of Hyaline Membrane Disease of the Newborn, Minnesota Med. **38**: 514, 1955.
8. Blystad, W., Landing, B. H., and Smith, C. A.: Pulmonary Hyaline Membrane in Newborn Infants; Statistical, Morphologic, and Experimental Study of Their Nature, Occurrence and Significance, Pediatrics **8**: 5, 1951.
9. Smith, C.: Symposium on Anoxia of the Newborn Infant, Oxford, 1953, Blackwell Scientific Publications.
10. Latham, E. F.: A Clinical Pathological Study of the Newborn Lung With Hyaline-like Membrane, Bull. Johns Hopkins Hosp. **96**: 173, 1955.
11. Rogers, W. S.: Hyaline Membrane in the Lungs of Premature Infants, Am. J. Obst. & Gynec. **71**: 9, 1956.
12. Gilmer, W. S.: Morphologic Studies of Hyaline Membrane in the Newborn Infant, A. M. A. Arch. Path. **59**: 207, 1955.
13. Haddad, H. M.: Studies on the Respiratory Rate in the Newborn, Pediatrics **17**: 204, 1956.
14. Silverman, W. A.: A Controlled Clinical Trial of the Effects of Water Mist on Obstructive Signs, Death Rate and Necropsy Findings Among Premature Infants, Pediatrics **17**: 1, 1956.
15. Blystad, W.: Hyaline Membrane Syndrome in Premature Infants, Arch. Dis. Child. **31**: 33, 1956.
16. Caffey, J.: Pediatric x-ray Diagnosis, Chicago, 1950, Year Book Publishers, Inc.
17. Donald, I., and Steiner, R. E.: Radiography in the Diagnosis of Hyaline Membrane, Lancet **2**: 846, 1953.
18. Petersen, H. G.: Contrasting Roentgenographic Pulmonary Patterns of Hyaline Membrane and the Fetal Aspiration Syndrome, Am. J. Roentgenol. **74**: 800, 1955.
19. Miller, H. C., and Behrle, F. C.: Effects of Hypoxia on the Respiration of Newborn Infants, Pediatrics **14**: 93, 1954.
20. Miller, H. C.: Hypoxia on the Respiration of Newborn Infants, Pediatrics **16**: 93, 1955.
21. Graham, B. D., and Wilson, J. L.: Chemical Control of Respiration in Newborn Infants, A. M. A. Am. J. Dis. Child. **87**: 287, 1954.
22. Blystad, W.: Blood Gas Determinations on Premature Infants. II. Investigations of Premature Infants With Early Neonatal Dyspnea, Acta. Ped. **45**: 103, 1956.
23. Howard, P. J., and Bauer, A. R.: Quantitative Variations in the Respiration of the Newborn Infant, A. M. A. Am. J. Dis. Child. **86**: 284, 1953.
24. Cook, C. D.: Studies of Respiratory Physiology in the Newborn Infant. Observation on Normal Premature and Full-Term Infants, J. Clin. Invest. **34**: 975, 1955.
25. Cook, C. D.: Respiratory Distress in the Newborn, New England J. Med. **254**: 562, 1956.
26. Drorbaugh, J. E.: "Vital Capacity" and Lung Compliance in Normal Newborn Infants and Infants With "Hyaline Membrane Syndrome," paper presented at 67th meeting of the American Pediatric Society, Carmel, June, 1957.
27. Fifth M & R Conference: Pulmonary Hyaline Membranes in Newborn Infants, Philadelphia, 1952, Ross Laboratories.
28. Schaffer, A. J.: Pathogenesis of Intrauterine Pneumonia, Pediatrics **17**: 747, 1956.
29. Barcroft, J.: Researches on Prenatal Life, Springfield, Ill., 1946, Charles C Thomas.
30. Farber, S., and Wilson, J. L.: The Hyaline Membrane in the Lungs, Arch. Path. **14**: 437, 1932.
31. Claireaux, A. E.: Hyaline Membrane in the Neonatal Lung, Lancet **2**: 749, 1953.
32. Lelong, R.: Symposia on Anoxia of the Newborn Infant, Oxford, 1953, Blackwell Scientific Publications.
33. Gellis, S. S., White, P., and Pfeffer, W.: Gastric Suction: A Proposed Additional Technic for Prevention of Asphyxia in Infants Delivered by Cesarian Section, New England J. Med. **240**: 533, 1949.
34. Freeman, L. C., and Scott, R. B.: Gastric Suction in Infants Delivered by Caesarian Section; Role in Prevention of Respiratory Complications, A. M. A. Am. J. Dis. Child. **87**: 570, 1954.
35. Reuther, L.: Hyaline Membrane and Atelectasis in the Lungs of Newborn Infants, Gynaecologia **137**: 367, 1954.
36. Ingalls, T. H.: Epidemiology of Retrolental Fibroplasia in Etiologic Relation to Pulmonary Hyaline Membrane, New England J. Med. **251**: 1017, 1954.
37. Bruns, P. D., and Shields, L. V.: Pathogenesis and Relationship of the Hyaline-like Pulmonary Membrane to Premature Neonatal Mortality, Am. J. Obst. & Gynec. **61**: 890, 1951.

38. McGregor, A. R.: Symposia on Anoxia of the Newborn Infant, Oxford, 1953, Blackwell Scientific Publications.
39. Arwaka, J. K.: Pulmonary Lesions in Experimental Oxygen Poisoning, A. M. A. J. Dis. Child. 91: 614, 1956.
40. Duran-Jorda, F.: A Histochemical Study of the Pulmonary Hyaline Membrane, Arch. Dis. Child. 31: 113, 1956.
41. Hadders, H. N.: On the Origin of the Pulmonary Hyaline Membrane, J. Path. & Bact. 70: 419, 1955.
42. Gitlin, D.: The Nature of the Hyaline Membrane in Asphyxia of the Newborn, Pediatrics 17: 64, 1956.
43. Laufe, L. E., and Stevenson, S. S.: Pulmonary Hyaline Membranes; Preliminary Report on Experimental Production, Obst. & Gynec. 3: 637, 1954.
44. Weiner, A. E., Reid, D. E., and Roby, C. C.: Hemostatic Activity of Amniotic Fluid, Science 110: 190, 1949.
45. Stevenson, S. S., and Laufe, L. E.: Experimental Production of the Pulmonary Hyaline Membrane Syndrome, J. PEDIAT. 47: 40, 1955.
46. Miller, H. C., Behrle, F. C., and Gibson, D. M.: Comparison of Pulmonary Hyaline Membrane in Vagotomized Rabbits With Those in Newborn Infants, Pediatrics 7: 611, 1951.
47. Miller, H. C., and Behrle, F. C.: Respiratory Patterns in Newborn Infants as Determined by Airflow and Pneumographic Studies and Their Possible Relationship to a Deficient Vagal Mechanism, Pediatrics 10: 272, 1952.
48. Lynch, M. J. G.: Hyaline Membrane Disease; Further Observations, J. PEDIAT. 48: 165, 1956.
49. Drinker, C. K.: Clinical Physiology of the Lungs, Springfield, Ill., 1954, Charles C Thomas.
50. Winter, W. D., Jr., and Gellis, S. S.: Pulmonary Hyaline Membranes in Infants of Diabetic Mothers, A. M. A. Am. J. Dis. Child. 87: 702, 1954.
51. Lendrum, F. C.: The Pulmonary Hyaline Membrane as a Manifestation of Heart Failure in the Newborn Infant, J. PEDIAT. 47: 149, 1955.
52. Polacek, K.: The Pathogenesis of Hyaline Membrane Disease; Etudes Neonatal, 5: 31, 1956.
53. Lynch, M. J. G.: Hyaline Membrane Disease of Newborn Premature Lungs, J. PEDIAT. 47: 275, 1955.
54. Lynch, M. J. G.: Hyaline Membrane Disease, Its Nature and Etiology, J. PEDIAT. 48: 602, 1956.
55. Potter, E. L.: Pulmonary Pathology in the Newborn, Advances in Pediatrics. VI. Chicago, 1953, p. 157.
56. Smith, C.: Physiology of the Newborn, Springfield, Ill., 1951, Charles C Thomas, p. 38.
57. Lind, A.: Human Fetal Circulation Changes in the Cardiovascular System at Birth and Disturbances in the Postnatal Closure of the Foramen Ovale and Ductus Arteriosus; Cold Spring Harbor Symposia on Quantitative Biology, 19, Baltimore, 1954, Monumental Printing Co.
58. James, L. S.: Changes in the Heart and Lungs at Birth, J. PEDIAT. 51: 95, 1957.
59. Rowe, R. D.: The Normal Pulmonary Arterial Pressure During the First Year of Life, J. PEDIAT. 51: 1, 1957.
60. Eldrige, F. L.: Physiologic Closure of the Ductus Arteriosus in the Newborn, J. Clin. Invest. 34: 987, 1955.
61. James, L. S.: The Pattern of Response of Pulmonary and Systemic Arterial Pressures in Newborn and Older Infants to Short Periods of Hypoxia, J. PEDIAT. 51: 5, 1957.
62. Adams, F. H.: Physiological Studies on the Cardiovascular Status of the Newborn Infant, Pediatrics 19: 431, 1957.
63. Jukka, S.: Mechanism of Initiation of Respiration in the Newborn, Acta paediat. 43 (supp. 100): 397, 1954.
64. Personal communication.
65. Personal communication.
66. Wagner, J. C.: Histochemistry of the Pulmonary Hyaline Membrane in Newborn Infants and Its Interpretation, Lancet 2: 634, 1954.
67. Miller, H. C.: The Pathogenesis of the "Vernix Membrane"; Relation to Aspiration in Stillborn and Newborn Infants, Pediatrics 3: 735, 1949.
68. Stadie, W. C., Riggs, B. C., and Haugaard, N.: Oxygen Poisoning, Am. J. M. Sc. 207: 84, 1944.
69. Szewczyk, T. S.: Retrolental Fibroplasia; Etiology and Prophylaxis, Am. J. Ophth. 35: 301, 1952.
70. Tran Dinh De, and Anderson, G. W.: Experimental Production of Pulmonary Hyaline-like Membranes With Atelectasis, Am. J. Obst. & Gynec. 68: 1557, 1954.
71. Silverman, W. A.: Controlled Clinical Trial on the Effects of Alevaire Mist on Premature Infants, J. A. M. A. 157: 1093, 1955.
72. Silverman, W. A.: The Effect of Humidity on Survival of Newly Born Premature Infants; paper presented at sixty-seventh meeting of the American Pediatric Society, Carmel, June, 1957.
73. Miller, H. C.: Indications for Oxygen Therapy in Small Premature Infants; paper presented at sixty-seventh meeting of the American Pediatric Society, Carmel, June, 1957.
74. Engle, M. A.: Response of Small Premature Infants to Restriction of Supplemental Oxygen, A. M. A. Am. J. Dis. Child. 89: 316, 1955.
75. Smith, C.: Neonatal Physiology for the Roentgenologist, Am. J. Roentgenol. 74: 791, 1955.

76. Gitlin, D.: The Obstructive Factors in the Pulmonary Hyaline Membrane Syndrome of Newborn Infants; paper presented at the twenty-seventh meeting of the Society for Pediatric Research, Carmel, June, 1957.
77. Bruns, P. D., and Shields, L. V.: High Oxygen and Hyaline-like Membranes, Am. J. Obst. & Gynec. **67**: 1224, 1954.
78. Miller, J. A.: Factors in Neonatal Resistance to Anoxia: Temperature and Survival of Newborn Guinea Pigs Under Anoxia, Science **110**: 113, 1949.
79. Silverman, W. A.: The Influence of Thermal Environment Upon Survival of Premature Infants in the First Five Days of Life; paper presented at the twenty-seventh meeting of The Society for Pediatric Research, Carmel, June, 1957.
80. Hamwich, A.: Mechanisms for the Maintenance of Life in the Newborn During Anoxia, Am. J. Physiol. **185**: 387, 1941.
81. Reardon, H. S.: Treatment of Acute Respiratory Distress in Newborn Infants of Diabetic and "Prediabetic" Mothers; paper presented at the twenty-seventh meeting of The Society for Pediatric Research, Carmel, June, 1957.
82. Goddard, R. F.: Newer Concepts of Infant Resuscitation and Positive Pressure Therapy in Pediatrics, A. M. A. Am. J. Dis. Child **89**: 70, 1955.
83. Day, L. R.: Electrophrenic Artificial Respiration in the Newborn, A. M. A. Am. J. Dis. Child. **89**: 553, 1955.
84. Love, W. G., Jr., and Tillery, B.: New Treatment for Atelectasis of the Newborn, A. M. A. Am. J. Dis. Child. **86**: 423, 1953.
85. Townsend, E. H.: Treatment of Atelectasis by Thoracic Traction, Pediatrics **17**: 250, 1956.

Comments on Current Literature

NATURAL IMMUNITY TO POLIOMYELITIS

THE acquisition and maintenance of natural immunity to poliomyelitis is a subject of importance even in the present era of basic immunization by trivalent vaccine. In this connection, extensive and in some respects unique investigations carried out recently in Louisiana are of interest. These include studies of entirely natural immunity in certain grouped households and observations on naturally occurring poliovirus infections in vaccinated children. Some of these studies by Fox, Gelfand, LeBlanc, Conwell and their associates were reported at the annual meeting of the American Public Health Association in Atlantic City in November, 1956. More complete reports appear in the *American Journal of Public Health*[1] for April, 1957, and in the *American Journal of Hygiene*[2, 3] for May, 1957.

Observations were initiated in 1953 on a group of approximately 150 newborn infants and their household associates residing in southeastern Louisiana for the purpose of ascertaining "the time when and the circumstances under which naturally acquired, primary immunizing infections with polioviruses occur."[2] In addition to interesting results obtained concerning the prevalence of virus, the occurrence under natural conditions of repeated immunizing infections, the development of antibodies to the three strains of poliovirus, etc., the constancy of the study population is an important and interesting feature of the investigation. Retention in the study of most of the original households was possible for the entire observation period, about 30 months, on the average. Only 21 of the original "households were lost from observation, despite the fact that continued participation involved real inconvenience of lengthy interviews, and such disagreeable features as collection of stools and blood specimens monthly from the index infant, and periodically from all household members."[2] Only four households withdrew from the study because of unwillingness to cooperate; most of the twenty-one households lost to observation were accounted for by family removal to some relatively distant point. This rather remarkable record is attributed by the authors to careful initial selection during the recruitment phase of the study, but more specifically to the continued efforts on the part of the nurse-epidemiologist of the group (LeBlanc) to sustain interest among the families involved, and to foster continued good rapport with their individual members.

The recruitment phase extended from April to November, 1953, the objective being to find and enlist households with newborn children which would remain relatively stable with respect to certain socioeconomic and other environmental factors. In most instances enlistment in the study was accomplished while the index child was still unborn. Over the study period from April, 1953 through 1955, the occurrence of natural (subclinical or completely silent) infection and the development of natural immunity to poliovirus were followed in these index children and their household contacts by serologic studies and by tissue culture methods for virus isolation. Virus isolation from stool specimens

was correlated closely with changes in titer of antibody to the three strains of poliovirus. No significant clinical disease was associated with 244 primary infections and 65 reinfections observed in this study. Minor illness seemed to be associated in about 27 per cent. Infections with all three strains of poliovirus occurred in children of all ages from about the age of 3 weeks, with no significant predilection for any particular age group. These infections, as evidenced by the presence of virus in fecal specimens, occurred throughout the year with a marked peak in the late summer period. The duration of fecal excretion following isolation was of the order of 50 days. In general, the increase in titer of neutralizing antibody correlated specifically with the type of virus isolated from the fecal specimens. There were, however, a few instances of variation from the usual pattern of neutralizing antibody development. Some of these variations in the appearance of antibody were to be expected, since it is impossible in a study of this kind to assign the precise day of infection. Some of the variations in antibody response consisted in delayed response, as in the case of one child whose fecal specimens yielded type I virus about six weeks before antibody rise to type I was significant. However, there was apparently no significant clinical illness in this child. In newborn infants there was little evidence that maternally derived antibody prevented silent infection; from the moment of birth apparently "the child is susceptible to infection with polioviruses and when infected responds with the production of specific antibody and with the excretion of the newly formed virus."[3] The somewhat lower infection frequencies in very young children during periods of household infection are explained by the authors on the basis of protection of the young infant from exposure.

There were differences in the types of polioviruses prevalent during the two complete study years, 1954 and 1955, and in various more restricted areas during any one year, type II poliovirus being the least evident as a general rule in silent immunizing infections, and also apparently deficient in virulent strains. The ease with which the polioviruses spread from person to person is emphasized by these authors, such spread being demonstrated in many instances during their study. Rapid spread within the family or household is the general rule; interhousehold spread usually occurs by way of intimate child contacts. It may affect the entire neighborhood with a fair degree of rapidity or spread more slowly. Two households five city blocks from each other experienced simultaneously infection with one virus type, and two months later simultaneous infection with another virus type. In summary, the authors present a concept of dissemination of polioviruses based entirely on data provided by this study. "Within a very large community, polioviruses of all three types are circulating continually. The volume of transmission as a whole is controlled seasonally by limitations on the intimacy of contact of the susceptible portion of the population, and is controlled within the different social strata by differences in the level of environmental sanitation and personal hygiene."[3] The authors believe that in communities where there is a high volume of subclinical and silent infection as in the area studied, "the accumulation of immunes has reached nearly 75 per cent by school age," and, excluding young infants, that "the most effective cohort of contact is the age group two to five years old. In this view, therefore, infection with poliovirus spreads through the community mainly in a horizontal manner from family to family via the young child population. This is followed by a secondary spread within each family in a vertical manner, upward to older siblings and adults . . . and downward to younger siblings who may not before have had the opportunity."[3]

In conjunction with the study of natural immunity to the viruses of poliomyelitis, this group of investigators has also studied the occurrence of natural poliovirus infections in vaccinated children. About 300 children belonging to 118 Louisiana households were found to be incompletely immune in that they lacked antibodies to one or more types of poliovirus. Accordingly these children were vaccinated by means of a two-inoculation primary course of Salk vaccine. Type-specific neutralizing antibody response was followed by measuring the ability of serum specimens to inhibit the cytopathogenic effect of standard strains of poliovirus in tissue culture. During the first seven months following vaccination, the children of these households were observed closely for the occurrence of alimentary infections with polioviruses. In the 118 households a total of forty household episodes was detected. These observations made after vaccination were compared with similar observations made previously on the same group before any vaccine inoculations had been carried out.

The authors conclude that this two-inoculation primary course of vaccine did not influence the frequency or the duration of silent infections with polioviruses, nor the quantity of virus excreted in the fecal specimens. They predict that the third booster inoculation will not alter this situation, the implication being that silent infections will continue to occur with regularity in vaccinated children, and that "... vaccines will not result in the gradual elimination of polioviruses from vaccinated areas."[1] Such well-documented long-term studies as these will go far toward elucidating the natural history of poliomyelitis and will contribute significantly to a better understanding of the role to be played by the broad immunization programs being undertaken currently.

RUSSELL J. BLATTNER

REFERENCES

1. Gelfand, Henry M., Fox, John P., and LeBlanc, Dorothy R.: Observations on Natural Poliovirus Infections in Immunized Children, Am. J. Pub. Health 47: 421, 1957.
2. Fox, John P., Gelfand, H. M., LeBlanc, D. R., and Conwell, Donald P.: Studies on the Development of Natural Immunity to Poliomyelitis in Louisiana: I. Over-all Plan, Methods and Observations as to Patterns of Seroimmunity in the Study Group, Am. J. Hyg. 65: 344, 1957.
3. Gelfand, H. M., LeBlanc, D. R., Fox, J. P., and Conwell, D. P.: Ibid., II. Description and Analysis of Episodes of Infection Observed in Study Group Households, Am. J. Hyg. 65: 367, 1957.

Correspondence

To the Editor:

The Pediatrician's Role in Society

Pediatrics, during the first half of this century, has been a brilliant part of our whirlwind social advance. Improved infant feeding, the abolition of the contagious scourges, and the understanding of growth and development have, with the coming of fantastic surgical techniques, been sufficient to nearly eliminate the need for large numbers of pediatric internists.

Rapid transportation and antibiotics have revolutionized our work. Gone is the day when it took a genius to feed a normal infant—our earlier gems of knowledge and techniques have fortunately become almost public knowledge. The rising level of education has made the ordinary routine of providing for an infant fairly simple. Mothers and their infants frequent well-baby clinics where their mutual needs are well met—the socialized and complete facilities available for children's medical care are now an integral part of most city living—leaving the board-trained pediatrician in an interesting, frustrating position.

I hope that those who have the responsibility for future resident training might mold the pediatric specialist of tomorrow with some of these changes in mind to allay some of the dissatisfactions that are evident in our field, judging from the numbers of pediatricians who annually bolt into greener pastures.

What is today's pediatrician for? What is wrong with today's system of postgraduate training that annually turns out scores of well-trained pediatricians who think that their fascinating work in the teaching hospitals and clinics is their guarantee of an interesting and stimulating office practice?

Rapid social and economic changes, particularly the way in which medicine is actually practiced, will often surprise and dismay the recent newcomer to pediatrics. Since the specialties have arrived, even in small towns, and especially the subspecialties in pediatrics, cardiology, radiology, otolaryngology, surgery (orthopedic, etc.), the pediatrician is indeed low man on the totem pole, his position comparable to that in which the general practitioner imagines himself, but without the satisfactions and interests of the generalist's broad attack on the whole of medical practice, not to mention his income from surgery and obstetrics. Well babies still frequent the pediatrist's office, but it is inconceivable that any physician with intelligence and interest in the unusual can long survive the routine of playing grandmother for years on end in a well-baby practice.

A few years ago this colorless job was relieved by challenges of frequent and severe disease, and the physician was continually called upon to exercise his greatest ingenuity. He felt deep satisfaction in his work, a satisfaction which is waning today because of the changed nature of our practice except in large centers where unusual cases congregate.

My former pediatric practice in a Northwest city is a good example. With a population of about 60,000, well supplied with competent general practitioners and top quality specialists, the daily routine was monotonous in the extreme. Upper respiratory infections, infant feeding, the endless discussions with endless mothers of problems that are self-righting anyhow—all of it except the occasional emergency situation was not sufficiently stimulating for a steady diet. There are no longer enough surprises in the package.

What is wrong? Is it the individual or the specialty that currently makes at least one third of pediatricians dissatisfied enough to wish themselves out of the practice of pediatric medicine? Perhaps it is

both. If the specialty is to continue unchanged, extreme care will be needed to make certain that those intending to do only pediatric office practice are aware of its enforced preoccupation with trivia largely unrelated to disease.

Few men will knowingly accept such a career—in time the specialty may lose the top quality men it has attracted in past years. The intern who contemplates a career in pediatric medicine must, I believe, be willing to look for realistic satisfaction in his work in one of two ways—either in the teaching hospital where he can well use the bulk of his training, or in some consultative position requiring knowledge of the field of pediatric medicine, such as public health planning or in some work such as assisting with hospital development in foreign countries, or full-time research. Pediatric medical office practice is not enough; there are too many private pediatric practices being started today that will be abandoned from sheer boredom.

Obviously we will continue to need top pediatric skill available for the seriously ill child, regardless of location or financial considerations. Since the pediatric internist is largely trained to meet the problems of whole families, it tends to fall to his lot to be the family doctor—whom families, surprisingly, still cherish. It is not a difficult step from pediatric practice to include the problems of the aged members of the family and to cover work that is considered to be the province of the family doctor of years ago, even to doing some surgery and obstetrics with adequate supervision and training. Many practicing pediatricians who are today complaining of monotony and relatively low income from their work do not realize that they are simply trying to do at a high cost what is being done well by the general physician and scores of social agencies, as well as by the popular publications which disseminate sound pediatric advice. Their work has largely been taken over by the rest of the medical world, which seems to be doing an excellent job of it.

The disgruntled pediatrician will find his world more pleasant if he will simply accept the fact that by widening his usefulness to society by including some general practice in his work, variety will again spice his life. This step is not unreasonable or awkward from an educational standpoint. Internal medicine is similarly contrived in principle for all age groups—the niceties of age difference are not unsurmountable to a discerning physician. Indeed the day may come when practicing physicians will no longer find it worth while to split the internist's field into age groups—the advances of knowledge are at last providing us with an integrated understanding of disease processes. I feel we have reached the end of schismatic medicine as it applies to the ordinary office practice; it is no longer necessary, nor is it emotionally or economically sound. At least one third of practicing pediatricians agree, since they have indicated their disgust for present pediatric practice as such.

Fortunately, the regulations of our Board do not limit a diplomate to the practice of pediatric medicine; they simply indicate special skills in that field. It is unfortunate that our diplomates are so commonly averse to any work of a more general nature, as many pediatricians would be much happier and of more value to society in *general practice with special attention to pediatrics.* It is my feeling that this type of practice could for many relieve the boredom of viewing the medical world from the inside of a diaper and at the same time assure them an adequate income (insurance plans being what they are).

It must be repeated that for many men in pediatrics today, no problem exists. The teachers, those in research and administrative work, those in certain practices with built-in satisfactions, as well as those other individuals to whom this article does not pertain, thanks to their personality types—all these physicians are at peace with their profession and will not add to the statistics of those who contemplate their lot with rancor. But for the rest, whose pattern of living demands something that is lacking in medicine for the average pediatric internist and for the men contemplating future pediatric practice in the intellectual mediocrity of suburbia, I recommend the enjoyment and rewards of general work by men fortified by their board training in pediatrics.

If pediatric internists are to function precisely as such, to be happy they must find their places in large centers, mainly as consultants, or in other fields where their knowledge is essential, and their talents are fully utilized. Routine pediatric office practice is today a dull anachronism.

It is sincerely hoped that the policy of the American Board of Pediatrics remains as it is at present, permitting a diplomate to include in his work any portion of the art of healing he finds interesting—thus encouraging the further development of our value to society, as it needs us, not as we think it should use our services.

FRANK L. TABRAH, M.D.

[Dr. Tabrah, who submitted the preceding communication, was, according to records, graduated from the University of Buffalo Medical School in 1943. He received his pediatric training at the Buffalo Children's Hospital and Children's Orthopedic Hospital in Seattle, and was certified by the American Board of Pediatrics. He was in pediatric practice in Bellingham, Washington, for several years. Last year he gave up his practice and joined the staff of the medical department of the Kohala Sugar Company, Kohala, Hawaii. He writes that the statement that "one third" of the pediatricians in practice are dissatisfied is based on an article in the November, 1956, issue of *Medical Economics*. Ed.]

Dr. Lee F. Hill, President of the American Board of Pediatrics, commented as follows on Dr. Tabrah's letter.

In his discussion, Dr. Tabrah makes two references to the American Board of Pediatrics. The first states that the regulations of the Board do not limit diplomates to the practice of pediatric medicine. This is correct. Since its inception in 1934, the Board has maintained the policy that its proper functions were (1) to establish standards for training, (2) to examine all candidates who met these training requirements, and (3) to issue its certificate to those who successfully passed its examination. Rescinding of a certificate would occur only under the circumstance that a diplomate had deliberately falsified his application record. The Board believes that "policing" of its duly qualified certicate holders with respect to their later conduct is not its responsibility but rather is that of other groups or organizations. Thus there is nothing in the present regulations or policy of the Board of Pediatrics which would prevent a certified pediatrician from including in his work "any portion of the art of healing he finds interesting."

In his second reference Dr. Tabrah hopes the policy of the Board will remain as it is at present. What the policy of the Board might be in the unlikely event that the future trend of pediatric practice followed some such pattern as suggested by Dr. Tabrah cannot, of course, be foretold. At present there is little to indicate that general interest in pediatrics as a specialty is on the wane. The Board of Pediatrics is the third largest among the 18 Boards, having now a membership exceeding 6,000. The Boards of Internal Medicine and Surgery only are larger. The number of pediatricians certified by the Board prior to the war averaged about 100 per year. The following table illustrates what has happened in recent years.

	APPLICATIONS RECEIVED	NUMBER EXAMINED
1951	390	391
1952	546	512
1952	502	509
1954	461	524
1955	457	476
1956	473	419
1957	482	500 (planned)

Applications for 1958 thus far exceed those for 1957 at the same date. These figures clearly indicate sustained interest in pediatrics as a specialty and suggest that dissatisfaction with practice is on an individual basis. One wonders if a poll of other specialties might not disclose a similar amount of dissatisfaction as that alleged for pediatrics.

LEE F. HILL

News and Notes

The **Sister Elizabeth Kenny Foundation** announces a continuance of its postdoctoral scholarships to promote work in the field of neuromuscular diseases. These scholarships are designed for scientists at or near the end of their fellowship training in either basic or clinical fields concerned with the broad problem of neuromuscular diseases.

Kenny Foundation Scholars will be appointed annually. Each grant provides a stipend of from $5,000 to $7,000 a year for a five-year period, depending upon the Scholar's qualifications. Candidates from medical schools in the United States and Canada are eligible.

Inquiries concerning details should be sent without delay to: Dr. E. J. Huenekens, Medical Director, Sister Elizabeth Kenny Foundation, 2400 Foshay Tower, Minneapolis 2, Minn.

A five-day program in *Pediatric Orthopedics* will be jointly presented by the Departments of Pediatrics and Orthopedics of **Tulane University School of Medicine** between the dates of Feb. 24 and 28, 1958. Dr. William T. Green of Harvard Medical School will assist the combined faculties in dealing with diagnostic and nonoperative features in the management of congenital disturbances, metabolic disorders (including orthopedic reflections of systemic disease), malignant and other bone tumors, cerebral palsy and allied conditions, and functional, postural, and developmental problems. Lectures as well as small group discussions of patients and round table seminars will be used in presenting material. As usual registration is restricted to forty qualified specialists.

Further information and applications may be secured from the Division of Graduate Medicine, Tulane Medical School, 1430 Tulane Avenue, New Orleans 12, La.

The **Public Health Service** has announced a new program of financial support for advanced training of research scientists in the field of neurological and sensory disorders.

A previous program, under which about 75 scientists received advanced training during the last fiscal year, was concerned exclusively with clinical training. The program announced today is designed to encourage advanced training in either the clinical area or in such basic science areas as neurochemistry, neuropharmacology, neurophysiology, or neuroanatomy.

Individual awards under the program generally will be made for not less than nine months and for not more than one year. However, all awards are subject to renewal and may be continued for a period of three years. Stipends are determined individually in accordance with each applicant's qualifications and training needs. Such stipends may range from $5,500 to $14,800 a year.

Application forms and instructions may be obtained by writing to the Chief, Extramural Programs Branch, National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda 14, Md. Completed applications should be submitted to the same address.

Applicants must be citizens of the United States or must have filed declarations of intent to become citizens. They must be free of any physical or mental disability that would interfere with the proposed training. In addition, they must have completed either (1) the residency training requirements in a clinical specialty, or its equivalent, or (2) at least three years of pertinent postdoctoral training or research experience.

Special traineeships may be awarded for training at any institution in the United States or abroad qualified to give the particular training desired by the applicant.

The trainee may begin training at any time within ten months of the date of his award. During the period of training, the trainee will not be permitted to carry on the private practice of medicine; he may engage only in such teaching, clinical, and research activities as are a prescribed part of his training program.

Books

The Placement of Adoptive Children. J. Richard Wittenborn, Springfield, Ill., 1957, Charles C Thomas. 189 pp. Price $4.75.

This book presents the findings of the author and his co-workers in an investigation of two questions: (1) How accurately and in what respects can the Yale Developmental Examination of Infant Behavior be employed to predict future development for adoptive children? (2) What characteristics of adoptive homes (placement) may be shown to be correlated with characteristics of adoptive children?

The author goes on to state that the discussion touched upon such matters as what can be predicted for the adoptive child, what can be predicted for the adoptive parents, and what can be predicted for the adoptive family. He also states, "We are particularly concerned with aspects of behavior which may be anticipated from a knowledge of the child's status on an examination for infant development and from a knowledge of the environmental conditions under which he lived."

It should be brought out that this investigation was an attempt to validate the use of the infant examination as an aid in the evaluation of infants being considered for adoptive placement and was not concerned with the validity of the infant examination as a basis for evaluating the developmental status of the infant.

In making this study, all infants who did not receive the first examination before they were 14 months of age were excluded, and since there were only a few children in adolescence at the time of the investigation these also were excluded, as were those in the first grade of school because of the possibility that this period of uncertainty and rapid change might upset the results. Testing, then, was done of the 5-year-olds who were old enough to test in a reliable manner and the 7-, 8-, and 9-year-olds who had passed the first grade but who were not yet involved in preadolescent changes. Finally, as a third sample, thirty-five children were used who lived with their true parents and who were examined as infants in anticipation of their attendance at the clinic nursery school.

In the course of this study the following statements were made. "Our data indicate that infants may be placed before the age of 3 months with as much satisfaction to the adoptive parents as those placed after the age of 3 months." This point is further elaborated by the statement, "Our data would suggest that in general, the earlier the child is placed adoptively the better his chances for optimal development."

As to knowledge of the two parents, the authors go on to state that this "cannot be a major guide to the child placement agency. Such knowledge is usually scant and unreliable. When present it is often difficult and hazardous to use as a basis for prediction."

Regarding the age of adoptive parents this interesting conclusion is reached. "The most reliable trend indicated that parents whose average age was in the thirties at the time of the child's adoption tended to have children with relatively high I.Q.'s. Although these data may suggest that parents who are in their thirties at the time of adoption can provide a more stimulating environment for the children than adoptive parents who are under 30 or over 40, this is not a necessary conclusion."

In the matter of matching adoptive parents with adoptive children the following conclusion was reached. "In our sample it would appear by elimination that the most important factors in satisfaction or dissatisfaction are bound up with the behavioral background for congeniality. Possibly the attitudes, the expectations, and the practices of parents as they interact with

the responses of children may be the most profitable focus for our attention."

On the question of placement of children in homes where there are already children, we find this interesting finding. "We see that adoptive children whose parents have a child of their own to be more compulsive and more phobic than adoptive children who are the only children of their adoptive parents." They further go on to suggest, "We examined this possibility and discovered that adoptive parents who have had a child of their own have a higher score for unsympathetic child-rearing practices (with respect to the adoptive child) than the adoptive parents who have not had children of their own."

After reviewing the data secured by a study of the three samples the reader is somewhat discouraged to find the conclusions to be essentially negative ones. However, these conclusions have been reached. "We have used all available facets of the infant examination and a wide variety of criteria of child development in the hope of finding some indication that the infant examination has a practically useful predictive validity. Our data provide no such indication." As to the second phase of the problem, they conclude, "The inter-relations between the various aspects of environment and the various aspects of development provided by these diverse sources are for the most part mutually consistent in their implications and lend themselves to a discussion of practices and problems in the placement of adoptive children." Dr. Wittenborn further states that "two kinds of value emerge from our investigation. The first kind is most explicit in the present report; i.e., most of our information is directly relevant to child placement practices and in general tends to encourage a trend or pattern of change already discernible in some agencies.

"The second kind of value which emerges from our investigation is less immediate. Since the work of child placement has been conducted without the aid of any substantial body of relevant research, appreciable incidental value accrues from our investigation merely because of the fact that it makes us explicitly and critically aware of the need for specific additional investigations." The book then concludes with a long series of specific research needs which would seem to be suggested by the studies.

In summary, then, this book raises more questions than it answers. It does provide a lot of interesting material for workers in the field of adoption and would seem to throw considerable doubt on the predictive value of an examination such as that known as the Yale Developmental Examination.

C. C. F.

Magnetic Removal of Foreign Bodies. Murdock Equen, M.D., Springfield, Ill., 1957, Charles C Thomas, 94 pages. Price $4.50.

A technical monograph on the removal of foreign bodies by the use of the Alnico magnet. Alnico was introduced for magnetic purposes by the General Electric Company in 1935 and consists of aluminum 8 parts, nickel 14, cobalt 25, copper 3, titanium 1, and iron 49. The magnet was first used in medicine in 1943, and since then has been used extensively. The author has made several modifications in the design of the unit. This monograph takes up in detail its use for removing metal bodies from the respiratory and gastrointestinal tracts.

Dermatologic Formulary, ed. 2. Frances Pascher, M.D., editor, New York, 1957, Hoeber-Harper, 172 pages. Price $4.00.

The formulary of the Skin and Cancer Unit of the New York University Hospital and Post-Graduate Medical School. There is an introduction by Dr. Sulzberger, professor of dermatology. Practical and useful.

Editor's Column

A JOURNAL OF PEDIATRICS FUND FOR FURTHERING PEDIATRICS

SINCE the spring of 1953 the Editorial Board and Publishers of the Journal have had under consideration setting aside each year a certain amount of the profits from the JOURNAL for the "furthering of pediatrics." Two years ago the Publishers approached the Board with a concrete plan, in which the use of the Fund was to be entirely in the hands of the Editorial Board, and an executive of The C. V. Mosby Company attended the meeting of the Board in May, 1956, to discuss the matter.

Throughout the past year the Board has given much thought as to how this Fund should be used. A number of suggestions have been carefully considered and rejected by the Board in an attempt to find a constructive use for the money without simply making it an addition to funds at present available for a number of worth-while purposes. At the annual meeting of the Board in June of this year some new ideas were suggested, which it was realized would take time to explore before adoption.

In the meantime, while these were under consideration, the Board decided to use the money available for the current year—1957—in bringing out in a volume the "Pediatric Profiles" which have been appearing to the JOURNAL over the past three years. Many have expressed the desire for such a volume. It will be sent this month to all paid subscribers of the JOURNAL with the compliments of the Editorial Board and the Publishers.

IS PEDIATRIC PRACTICE A SATISFYING LIFEWORK?

A few month ago an editorial by Dr. Arthur H. Parmelee, Sr., describing the rewards of pediatric practice, was published in the *Bulletin of the Los Angeles Childrens Hospital*. With the kind permission of Dr. Parmelee and the *Bulletin*, the editorial follows. It is, we believe, one of the best answers to correspondence recently received from a younger pediatrician, personally unknown to us, and published in this issue (p. 745), who complains that he has not found satisfaction in the practice of pediatrics. It is not the first time that similar complaints have come to our attention. The question always comes up as to whether the "dissatisfaction" arises from what constitutes present-day pediatric practice, or lies in the personality of the dissatisfied individual. As regards the "Board" matters which are brought in, we have asked Dr. Lee F. Hill, president of the Board since 1955, to comment.

Pediatric Rewards

A. H. PARMELEE, SR., M.D.

Pediatricians in general are often ascribed distinguishing characteristics, and their gatherings seem somehow distinctive compared to those of other specialties. These characteristics are difficult to define precisely, but they may be described, I think, as gentleness, friendliness, thoughtfulness, trustfulness, respectfulness and a sense of humor. The special character of the pediatrician might be summarized as the poise of a sound philosophy pervaded by optimism.

Why should pediatricians have these qualities in greater measure than members of other specialties? Part of the answer is implied in another question. What causes certain people to choose pediatrics in preference to another specialty? It is not difficult to understand why some prefer not to specialize in surgery or obstetrics. Individual aptitudes, skills or personal inclinations may be decisively important; but why pediatrics in preference to internal medicine or one of its sub-specialties? It may be a simple chain of fortuitous circumstances. The reasons for my own choice are not easy to define precisely. I had been an assistant to an internist for a year. I enjoyed internal medicine, but not the limitations of being an assistant. When I entered independent general practice, my total ignorance of infant care became painfully obvious within a very short time. I was disturbed, and particularly so, because I was soon to become a father, and I read everything I could find on the subject. I learned the truth of a statement by my professor of psychology in college that interest and attention are synonymous. The more attention I gave, the greater my interest, and vice versa. The choice of pediatrics in my case resulted from this endless chain of interest and attention. Circumstances of chance undoubtedly decide the choice of a specialty frequently Often, too, the forces compelling a choice are subtle and unclear. But one thing is certain: no sane young physician would deliberately choose pediatrics for its financial rewards! There must then be something else. I like to believe that inherent individual qualities and environmental influences both play a role. The potential pediatrician has, I believe, an inherent mutual attraction to children and child life. I believe also that those who choose pediatrics are often influenced by the character of pediatricians they have known: teachers in medical school perhaps, hospital staff members or even the family pediatrician. If such contacts are decisive, what made these pediatricians attractive to the neophyte?

This brings us to the heart of our subject. It cannot be expected that those just starting their careers will foresee the rewards which are by-products of pediatric practice. Only those who have enjoyed these rewards can make others aware of them.

From a medical point of view, of course, the unique attractions of our specialty are readily recognized. Pediatrics can be defined as that branch of medicine concerned with health and disease as influenced by factors of growth and development. An understanding of human growth and development in all its physical, physiological, psychological, and social aspects is, in itself, fascinating. In addition, nowhere except in infancy and childhood do we see disease in pure form, unmodified by pre-existing pathologic processes. Where else can we see so vividly the effects of inadequate nutrition or of abnormal metabolism? Where else do we observe so clearly the results of intelligent therapy? Pediatrics offers relatively new and exciting fields for research. Great opportunities are still unfulfilled in study of the newborn, of genetics, and of adolescence.

It is not to these attractions that I particularly call your attention, however. I wish rather to emphasize the day to day privilege of watching children grow and develop from birth to adulthood, noting their characteristics at various stages and under varying environmental circumstances; the privilege of seeing them in their homes, knowing their families, home life, domestic trials; the privilege of sharing their happiness and their problems and observing their reactions. These and many other similarly rewarding experiences belong uniquely to the pediatrician and perhaps the general practitioner, to whom we are closely akin. No other profession, not even the clergy, quite shares our enviable position. In fact we are, in many respects, both physicians and clergymen. Catholic parents, without realizing their mistake, have often said to me: "Thank you, Father," or "Good-bye, Father." Our specialty gives a privileged position not only to know about children, parents, families and, in the long run, about people and the social structure, but also to learn from children and parents and families.

The lessons we can learn from children are many and they are delightfully taught. We learn very early that they recognize a friend when they see one; they read you like a book, even in infancy. No one responds to friendliness and understanding like a child, and no one detects sham more certainly and resents it more profoundly. Children have an uninhibited and completely disarming honesty in conversation. Let me recall some examples. I had my first wrist watch in 1922. Before World War I, wrist watches for men were almost unknown. I was definitely self-conscious about mine. The very first day I wore it in the office—yes, you guessed it—a six year old boy spotted it and said: "Look Mommy, Dr. Parmelee has a wrist watch just like a lady!". . . A boy of about six years was brought to me, whom I cared for as an infant and young child but whom I had not seen for more than a year because his family had moved to another part of Chicago. When he entered my office, he looked up at his mother and said: "I'm not going to tell Dr. Parmelee about the other doctor we went to, am I, Mother?" His mother could only say: "I hoped you weren't.". . . I called to see a nine year old boy. After my examination, while I was talking to the parents, his fourteen year old brother suddenly observed: "That's a new suit, isn't it?" I answered: "Yes, do you like it?" He reflected a moment and then said: "The pants are a little too long.". . . I had just examined a boy of five who was talking to his mother when suddenly, apropos of nothing in our conversation, he interrupted: "Dr. Parmelee, Dr. Parmelee." "Yes, what is it John?" "My Mommy is older than my Daddy. She's 37 and he's only 33." Such experiences help make pediatric practice fun and satisfying.

Children are keenly aware of appreciation of their intelligence and personal dignity. One learns to meet them on a level commensurate with their age, as person to person, and never to talk down to them. I knew a pediatric psychiatrist of fine professional standing who called every young boy "Butch" and every girl "Sis." Needless to say, he had difficulty in establishing rapport. Children detect affectation with clairvoyant accuracy. I cherish highly the compliment of a nine year old boy: "There's a fellow who knows how to talk to a guy."

We also learn to be honest and scrupulously fair in our relationships with children. They have a highly developed sense of fair play. It is difficult for them to forgive injustice. Fifteen years after the event, when the name of a young man's grade school teacher came up in conversation, he remarked: "I don't like her." When asked why, his answer was: "One day in school she accused me of something I didn't do and punished me for it.". . . A six year old patient of mine, son of a close doctor friend and a colleague, entered

the hospital for a tonsillectomy which I had advised and had discussed with him in advance. At the last minute, his father decided to have him circumcised at the same time. The boy was not told. Later, he refused to speak to either of his parents for more than a week. His trust had been betrayed.

Parents teach us too. We see them cope with their problems, and we appreciate the personal qualities that determine their success. One develops profound admiration for the courage, ingenuity and loyalty of parents in trying situations. My experiences with young wives of men in the armed forces and mothers of young children during World War II aroused tremendous respect and faith in the young people of this generation.

Dealing with all kinds of parents under all manner of circumstances over the years, we learn about people in a real and intimate way. It's a longitudinal study of people from a cross section of society.

There are the rewards of friendships, unique friendships based on mutual understanding from long and intimate association. Friendships of parents and of children. I think of those young boys and girls who have sought my advice about personal problems long after they had outgrown my care. They regarded me as a trusted friend. And I recall my thrill when a young woman whom I had cared for since birth chose me to care for her own first child. I have had that experience many times subsequently, but it never ceases to give me joy.

Yes, there are many reasons why pediatricians share qualities which distinguish them as a group from their colleagues in other medical specialties. Another important factor may be the much greater proportion of time we spend with women and children. Certain feminine and childish characteristics rub off on us, perhaps. I believe that's good! It's conducive to a well-rounded philosophy of living.

Many who read this have long been aware of these and other pediatric rewards. To some, this reminder may be a stimulus to a waning interest. To others, it may constitute a caution against "assembly line" practice, lest these lasting compensations pass them by.

My attention was recently directed to a survey in the November, 1950, issue of "Medical Economics" which indicated that 95 per cent of practicing pediatricians are glad they selected medicine as a career. But only 63 per cent of them were satisfied with their chosen specialty. Pediatrics had the smallest proportion of satisfied practitioners. The complaints could be summed up as low pay, long hours, too much work required in order to make an adequate living, too many house calls and too many phone call interruptions. What pediatrician has not had moments of feeling similarly abused? The comments of those who were satisfied with pediatrics as a specialty plainly indicated recognition of intangible compensations of sufficient value to justify their efforts. At first blush, this report might seem disturbing. But I think it is heartening to know that nearly two-thirds of our pediatric colleagues recognize the worth of these rewards. Their sizeable majority insures the distinctive tone that characterizes pediatric group meetings.

We pay for whatever we get in one way or another. It is a truism well worth periodic reconsideration. Compensations in lasting personal satisfaction should more than justify the attendant sacrifice.

INDEX TO VOLUME 51

AUTHORS INDEX*

A

ABBEY, JOSEPH A. (WITH TEVETOĞLU, FETHI), Chlorpromazine in pediatric surgery, 181

ADAMS, FORREST H., The early definitive diagnosis of patients with congenital heart disease, 202

— (WITH HOLVE, LESLIE M.), The early diagnosis of patent ductus arteriosus, 164

ANTONIUS, N. A. (WITH SIDERIDES, L. E., AND RICHLAN, A.), Unusual auricular flutter in newborn infant, 435

AOYAMA, SHIGETO (WITH CARTER, FRANK H., JR., MERCER, ROBERT D., AND KOLFF, WILLEM J.), Hemodialysis in children, 125

AREY, JAMES B. (WITH MCELFRESH, ARTHUR E.), Generalized cytomegalic inclusion disease, 146

ARIZTÍA, ANÍBAL, BUSTAMANTE, WERNER, MORENO, LUIS, DOBERTI, ARMANDO, ROMÁN, CLARA, PIZZI, TULIO, AND DÍAZ, MARÍA, Interstitial plasma cell pneumonia and Pneumocystis carinii, 639

B

BAHN, ROBERT C. (WITH FEINERMAN, BURTON, AND BURKE, EDMUND C.), The nephrotic syndrome associated with renal vein thrombosis, 385

BAIN, G. O., WANG, G. C., AND MISANIK, L. F., Giant cell hepatitis associated with hereditary spherocytosis, 549

BAKER, DAVID (WITH BARNESS, LEWIS A., GUILBERT, PAUL, TORRES, FRANCISCO E., AND GYÖRGY, PAUL), Nitrogen metabolism of infants fed human and cow's milk, 29

BAKWIN, HARRY, Child care in Russia, 313

BARNESS, LEWIS A., BAKER, DAVID, GUILBERT, PAUL, TORRES, FRANCISCO E., AND GYÖRGY, PAUL, Nitrogen metabolism of infants fed human and cow's milk, 29

— (WITH CORNELY, DONALD A., AND GYÖRGY, PAUL), Effect of lactose on nitrogen metabolism and phenol excretion in infants, 40

BARRY-LEDEAUX, SALLY (WITH NEMIR, ROSA LEE, AND ROBERTS, PAUL H.), Observations of antistreptolysin-O, C-reactive protein and electrophoretic protein patterns in maternal and neonatal sera, 493

BARSKY, PERCY, AND BEALE, A. J., The transplacental transmission of poliomyelitis, 207

BEALE, A. J. (WITH BARSKY, PERCY), The transplacental transmission of poliomyelitis, 207

BEHREE, M. R. (WITH GOLDRING, D., THOMAS, W. A., MCCOY, E., AND O'NEAL, R. M.), Clinical and pathological observations in infants with coarctation of the aorta and patent ductus arteriosus, 18

BENNETT, CLAUDE E. (WITH EDWARDS, WALTON M.), Anomaly of the inferior vena cava, 453

BERMAN, EDWARD J., AND KAHN, ALEXANDER J., Pulmonary interstitial emphysema with air-block syndrome, 457

BLATTNER, RUSSELL J., Agenesis of the spleen, 350

—, Intrauterine fetal oxygenation, 115

—, Mumps virus and subacute thyroiditis, 483

—, Natural immunity to poliomyelitis, 742

—, Recent developments in the study of measles virus, 611

—, Severe infections in splenectomized infants and children, 223

BREESE, B. B., AND DISNEY, FRANK A., A comparison of intramuscular and oral benzathine penicillin G in the treatment of streptococcal infections in children, 157

BROWN, BERTRAM S., Serum Akerfeldt test for schizophrenia in children, 46

BURKE, EDMUND C. (WITH FEINERMAN, BURTON, AND BAHN, ROBERT C.), The nephrotic syndrome associated with renal vein thrombosis, 385

BUSTAMANTE, WERNER (WITH ARIZTÍA, ANÍBAL, MORENO, LUIS, DOBERTI, ARMANDO, ROMÁN, CLARA, PIZZI, TULIO, AND DÍAZ, MARÍA), Interstitial plasma cell pneumonia and Pneumocystis carinii, 639

*July, pp. 1-124; August, pp. 125-232; September, pp. 233-362; October, pp. 363-492; November, pp. 493-620; December, pp. 621-754.

BUTZ, WILLIAM C. (WITH SHINABERGER, JAMES H., AND TOMSOVIC, EDWARD J.), Fatal acute appendicitis in a fifteen-day-old infant, 422

C

CARTER, FRANK H., JR., AOYAMA, SHIGETO, MERCER, ROBERT D., AND KOLFF, WILLEM J., Hemodialysis in children, 125

CINER, ERDOGAN (WITH LEE, CHI HAO), Congenital leukemia associated with mongolism, 303

COHEN, PHILIP (WITH KOZINN, PHILIP J., AND WIENER, HARRY), Infantile amaurotic family idiocy, 58

CONE, THOMAS E., JR. (WITH PEARSON, HOWARD A.), Anhidrotic ectodermal dysplasia with vascular purpura, 306

CORNELY, DONALD A., BARNESS, LEWIS A., AND GYÖRGY, PAUL, Effect of lactose on nitrogen metabolism and phenol excretion in infants, 40

CRAVIOTO, JOAQUÍN (WITH GÓMEZ, FEDERICO, RAMOS-GALVÁN, RAFAEL, FRENK, SILVESTRE, DE LA PEÑA, CARMEN, MORENO, MARÍA ELENA, AND VILLA, MARÍA ELENA), Influence of L-lysine supplements on the absorption and retention of nitrogen from milk by children with protein malnutrition, 262

CRAWLEY, JAMES W., Three cases of the juvenile form of amaurotic family idiocy (Vogt-Spielmeyer disease) with electroencephalographic findings, 571

CRUMP, E. PERRY, HORTON, CARRELL P., MASUOKA, JITSUICHI, AND RYAN, DONNALDA, Growth and development. I. Relation of birth weight in Negro infants to sex, maternal age, parity, prenatal care, and socioeconomic status, 678

CURTIS, PAUL, Hyaline membrane disease, 726

D

DACANAY, ELEONORA (WITH MATHESON, A., ROSENBLUM, ARTHUR, AND GLAZER, RICHARD), Local tissue and blood eosinophils in newborn infants, 502

DAVIS, JOHN B. (WITH TIETZ, K. GEORGE), Ruptured ovarian cyst in a newborn infant, 564

DAVISON, WILBURT C., Correspondence, 486

DE BRUIJNE, J. I., VAN CREVELD, S., AND STEENDIJK, R., WITH THE TECHNICAL ASSISTANCE OF GROEN, P. E., Surgical treatment of pyloric stenosis in an infant with hemophilia A, 698

DEGNAN, THOMAS J., Idiopathic hypoproteinemia, 448

DE LA PEÑA, CARMEN (WITH GÓMEZ, FEDERICO, RAMOS-GALVÁN, RAFAEL, CRAVIOTO, JOAQUÍN, FRENK, SILVESTRE, MORENO, MARÍA ELENA, AND VILLA, MARÍA ELENA), Influence of L-lysine supplements on the absorption and retention of nitrogen from milk by children with protein malnutrition, 262

DÍAZ, MARÍA (WITH ARIZTÍA, ANÍBAL, BUSTAMANTE, WERNER, MORENO, LUIS, DOBERTI, ARMANDO, ROMÁN, CLARA, AND PIZZI, TULIO), Interstitial plasma cell pneumonia and Pneumocystis carinii, 639

DISNEY, FRANK A. (WITH BREESE, B. B.), A comparison of intramuscular and oral benzathine penicillin G in the treatment of streptococcal infections in children, 157

DOBERTI, ARMANDO (WITH ARIZTÍA, ANÍBAL, BUSTAMANTE, WERNER, MORENO, LUIS, ROMÁN, CLARA, PIZZI, TULIO, AND DÍAZ, MARÍA), Interstitial plasma cell pneumonia and Pneumocystis carinii, 639

DODD, KATHARINE (WITH JOHNSON, NORMAN J.), Obstruction to left atrial outflow by a supravalvular stenosing ring, 190

DUNGAN, WILLIAM T., AND MCKEY, ROBERT M., JR., Low cerebrospinal fluid glucose associated with meningeal neoplasia, 186

E

EAMES, THOMAS H., Frequency of cerebral lateral dominance variations among school children of premature and full-term birth, 300

EDWARDS, WALTON M., AND BENNETT, CLAUDE E., Anomaly of the inferior vena cava, 453

EHRLICH, ROBERT M., Ectopic and hypoplastic pituitary with adrenal hypoplasia, 377

EISENBERG, LEON, Progress in neuropsychiatry, 334

ETTELDORF, JAMES N. (WITH HUGHES, WALTER T., JR.), Oropharyngeal tularemia, 363

F

FALK, WALTER (WITH LEVY, DAVID), Urinary calculus disease among Israeli immigrant and Arab children, 404

FAULKNER, JANE BULLOCK (WITH SHETLAR, M. R., PAYNE, R. W., AND STRENGE, HENRY B.), Objective evaluation of patients with rheumatic diseases. III. Comparison of serum glycoprotein, seromucoid, and C-reactive protein determinations as methods for the evaluation of patients with rheumatic fever, 510

FEINERMAN, BURTON, BURKE, EDMUND C., AND BAHN, ROBERT C., The nephrotic syndrome associated with renal vein thrombosis, 385

FERGUSON, ANGELLA D., TEIXEIRA, GERTRUDE C., AND SCOTT, ROLAND B., Novobiocin in common pediatric infections, 655

FISCHER, CARL C., The pediatrician and his changing world, 593

FRENK, SILVESTRE (WITH GÓMEZ, FEDERICO, RAMOS-GALVÁN, RAFAEL, CRAVIOTO, JOAQUÍN, DE LA PEÑA, CARMEN, MORENO, MARÍA ELENA, AND VILLA, MARÍA ELENA), Influence of L-lysine supplements on the absorption and retention of nitrogen from milk by children with protein malnutrition, 262

FRIERSON, HENRY F., HAWK, JOHN C., JR., AND JENKINS, MARGARET Q., Sporadic cretinism with goiter occurring in identical twins, 704

G

GARDNER, JOSEPH E., AND TEVETOĞLU, FETHI, The roentgenographic diagnosis of geophagia (dirt-eating) in children, 667

GILBERT, ENID F., RICE, E. CLARENCE, AND GREGORY, KRIKOR O., Paper electrophoretic study of serum proteins in children with leukemia, 238

GIRDANY, BERTRAM R. (WITH HANSMAN, CHARLOTTE F.), The roentgenographic findings associated with neuroblastoma, 621

GLAZER, RICHARD (WITH MATHESON, A., ROSENBLUM, ARTHUR, AND DACANAY, ELEONORA), Local tissue and blood eosinophils in newborn infants, 502

GOLDRING, D., BEHRER, M. R., THOMAS, W. A., MCCOY, E., AND O'NEAL, R. M., Clinical and pathological observations in infants with coarctation of the aorta and patent ductus arteriosus, 18

GOLDRING, DAVID (WITH STROMINGER, DONALD B., AND JAMES, DAVID H.), Constant infusion pump for limiting fluids, 310

GÓMEZ, FEDERICO, RAMOS-GALVÁN, RAFAEL, CRAVIOTO, JOAQUÍN, FRENK, SILVESTRE, DE LA PEÑA, CARMEN, MORENO, MARÍA ELENA, AND VILLA, MARÍA ELENA, Influence of L-lysine supplements on the absorption and retention of nitrogen from milk by children with protein malnutrition, 262

GONNE, WILLIAM S. (WITH NICHAMIN, SAMUEL J.), Foreign body (paper clip) in the esophagus of a young infant, 197

GREENBLATT, JACOB, Correspondence, 118

GREGORY, KRIKOR O. (WITH GILBERT, ENID F., AND RICE, E. CLARENCE), Paper electrophoretic study of serum proteins in children with leukemia, 238

GROEN, P. E. (WITH DE BRUIJNE, J. I., VAN CREVELD, S., AND STEENDIJK, R.), Surgical treatment of pyloric stenosis in an infant with hemophilia A, 698

GUILBERT, PAUL (WITH BARNESS, LEWIS A., BAKER, DAVID, TORRES, FRANCISCO E., AND GYÖRGY, PAUL), Nitrogen metabolism of infants fed human and cow's milk, 29

GUNDY, JOHN E., Acellular bacterial antigen complex (Hoffmann) in the treatment of children with recurrent respiratory infections and infectious asthma, 516

GYÖRGY, PAUL (WITH BARNESS, LEWIS A., BAKER, DAVID, GUILBERT, PAUL, AND TORRES, FRANCISCO E.), Nitrogen metabolism of infants fed human and cow's milk, 29

— (WITH CORNELY, DONALD A., AND BARNESS, LEWIS A.), Effect of lactose on nitrogen metabolism and phenol excretion in infants, 40

H

HANSEN, HOWARD (WITH KOCH, RICHARD), Treatment of acute purulent meningitis with tetracycline, 65

HANSMAN, CHARLOTTE F., AND GIRDANY, BERTRAM R., The roentgenographic findings associated with neuroblastoma, 621

HAWK, JOHN C., JR. (WITH FRIERSON, HENRY F., AND JENKINS, MARGARET Q.), Sporadic cretinism with goiter occurring in identical twins, 704

HILL, LEE F., The pediatrician's role in society (corr.), 745

HOGAN, WILLIAM, AND LIEBNER, EDWIN J., Familial fibrous swelling of the jaws, 554

HOLVE, LESLIE M., AND ADAMS, FORREST H., The early diagnosis of patent ductus arteriosus, 164

HORTON, CARRELL P. (WITH CRUMP, E. PERRY, MASUOKA, JITSUICHI, AND RYAN, DONNALDA), Growth and development. I. Relation of birth weight in Negro infants to sex, maternal age, parity, prenatal care, and socioeconomic status, 678

HUGHES, JAMES G., Apparent sensitization to novobiocin, 664

HUGHES, WALTER T., JR., AND ETTELDORF, JAMES N., Oropharyngeal tularemia, 363

J

JACOBZINER, HAROLD, Correspondence, 226

JAMES, DAVID H. (WITH STROMINGER, DONALD B., AND GOLDRING, DAVID), Constant infusion pump for limiting fluids, 310

JAMES, L. S., Changes in the heart and lungs at birth, 95

— AND ROWE, RICHARD D., The pattern of response of pulmonary and systemic arterial pressures in newborn and older infants to short periods of hypoxia, 5

— (WITH ROWE, RICHARD D.), The normal pulmonary arterial pressure during the first year of life, 1

JENKINS, MARGARET Q. (WITH FRIERSON, HENRY F., AND HAWK, JOHN C., JR.), Sporadic cretinism with goiter occurring in identical twins, 704

JENSEN, ADRIAN R., MARTIN, LESTER W., AND LONGINO, LUTHER A., Digital neurofibrosarcoma in infancy, 566

JOHNSON, NORMAN J., AND DODD, KATHARINE, Obstruction to left atrial outflow by a supravalvular stenosing ring, 190

K

KAHN, ALEXANDER J. (WITH BERMAN, EDWARD J.), Pulmonary interstitial emphysema with air-block syndrome, 457

KENDIG, EDWIN L., JR., BCG vaccination in Virginia, 54

KIEFER, JOSEPH N. (WITH PINTO, PETER S.), Infarction of the testicle in the newborn infant, 80

KIRAGUS, CHAHNOUR (WITH STORER, JOHN), Considerations on an unrecognized mediastinal cyst, 194

KOCH, RICHARD, AND HANSEN, HOWARD, Treatment of acute purulent meningitis with tetracycline, 65

KOHLER, COLETTE M. (WITH MUNSLOW, RALPH A., STOVALL, VIRGINIA S., AND PRICE, RICHARD D.), Brain abscess in infants, 74

KOLFF, WILLEM J. (WITH CARTER, FRANK H., JR., AOYAMA, SHIGETO, AND MERCER, ROBERT D.), Hemodialysis in children, 125

KOZINN, PHILIP J., WIENER, HARRY, AND COHEN, PHILIP, Infantile amaurotic family idiocy, 58

KRAMER, IRVING, AND SHERRY, S. NORMAN, The time of passage of the first stool and urine by the premature infant, 373

KRAUS, MICHAEL, AND WHITE, HARVEY, Congenital tracheoesophageal fistula in the neck without atresia, 580

L

LEE, CHI HAO, AND CINER, ERDOGAN, Congenital leukemia associated with mongolism, 303

LEE, R. (WITH PANSKY, B.), Niemann-Pick disease in a boy of 16 months, 290

LEVY, DAVID, AND FALK, WALTER, Urinary calculus disease among Israeli immigrant and Arab children, 404

LIEBNER, EDWIN J. (WITH HOGAN, WILLIAM), Familial fibrous swelling of the jaws, 554

LIVINGSTON, SAMUEL, The social management of the epileptic child and his parents, 137

LONGINO, LUTHER A. (WITH JENSEN, ADRIAN R., AND MARTIN, LESTER W.), Digital neurofibrosarcoma in infancy, 566

M

MARGILETH, A. M., Comparison of ocular reactions using penicillin and bacitracin ointments in ophthalmia neonatorum prophylaxis, 646

MARTIN, LESTER W. (WITH JENSEN, ADRIAN R., AND LONGINO, LUTHER A.), Digital neurofibrosarcoma in infancy, 566

MASUOKA, JITSUICHI (WITH CRUMP, E. PERRY, HORTON, CARRELL P., AND RYAN, DONNALDA), Growth and development. I. Relation of birth weight in Negro infants to sex, maternal age, parity, prenatal care, and socioeconomic status, 678

MATHESON, A., ROSENBLUM, ARTHUR, GLAZER, RICHARD, AND DACANAY, ELEONORA, Local tissue and blood eosinophils in newborn infants, 502

MATSANIOTIS, NICHOLAS S., Studies on protein metabolism in undernourished infants and children, 267

MCCOY, E. (WITH GOLDRING, D., BEHRER, M. R., THOMAS, W. A., AND O'NEAL, R. M.), Clinical and pathological observations in infants with coarctation of the aorta and patent ductus arteriosus, 18

MCCUE, CAROLYN MOORE, Steroid therapy for rheumatic fever, 255

MCELFRESH, ARTHUR E., Hemophilia, 474

— AND AREY, JAMES B., Generalized cytomegalic inclusion disease, 146

MCKEY, ROBERT M., JR. (WITH DUNGAN, WILLIAM T.), Low cerebrospinal fluid glucose associated with meningeal neoplasia, 186

MCLELLAN, M. S., AND WEBB, C. H., Ear studies in the newborn infant, 672

MERCER, ROBERT D. (WITH CARTER, FRANK H., JR., AOYAMA, SHIGETO, AND KOLFF, WILLEM J.), Hemodialysis in children, 125

MEYER, JOHN L., II, Congenital defect in the musculature of the stomach resulting in spontaneous gastric perforation in the neonatal period, 416

MILLER, ALVIN A., Congenital sulfhemoglobinemia, 233

MILLER, WALTER R., Observations on the examination of children's feet, 527

MISANIK, L. F. (WITH BAIN, G. O., AND WANG, G. C.), Giant cell hepatitis associated with hereditary spherocytosis, 549

MITCHELL, SHIELA C., The ductus arteriosus in the neonatal period, 12

MORENO, LUIS (WITH ARIZTÍA, ANÍBAL, BUSTAMANTE, WERNER, DOBERTI, ARMANDO, ROMÁN, CLARA, PIZZI, TULIO, AND DÍAZ, MARÍA), Interstitial plasma cell pneumonia and Pneumocystis carinii, 639

MORENO, MARÍA ELENA (WITH GÓMEZ, FEDERICO, RAMOS-GALVÁN, RAFAEL, CRAVIOTO, JOAQUÍN, FRENK, SILVESTRE, DE LA PEÑA, CARMEN, AND VILLA, MARÍA ELENA), Influence of L-lysine supplements on the absorption and retention of nitrogen from milk by children with protein malnutrition, 262

MUHLER, JOSEPH C. (WITH SCHWEINSBERGER, RICHARD A.), Urinary excretion of fluoride by children aged two through five years using a stannous fluoride-containing dentifrice in a natural fluoride area and a nonfluoride area, 634

MUNSLOW, RALPH A., STOVALL, VIRGINIA S., PRICE, RICHARD D., AND KOHLER, COLETTE M., Brain abscess in infants, 74

N

NEMIR, ROSA LEE, ROBERTS, PAUL H., AND BARRY-LEDEAUX, SALLY, Observations of antistreptolysin-O, C-reactive protein and electrophoretic protein patterns in maternal and neonatal sera, 493

NICHAMIN, SAMUEL J., AND GONNE, WILLIAM S., Foreign body (paper clip) in the esophagus of a young infant, 197

NISENSON, AARON, Seborrheic dermatitis of infants and Leiner's disease: a biotin deficiency, 537

O

O'NEAL, R. M. (WITH GOLDRING, D., BEHREE, M. R., THOMAS, W. A., AND MCCOY, E.), Clinical and pathological observations in infants with coaretation of the aorta and patent ductus arteriosus, 18

P

PANSKY, B., AND LEE, R., Niemann-Pick disease in a boy of 16 months, 290

PARMELEE, A. H., SR., Pediatric rewards (editorial), 752

—, Profile of Isaac Arthur Abt, 107

PAYNE, R. W. (WITH SHETLAR, M. R., STRENGE, HENRY B., AND FAULKNER, JANE BULLOCK), Objective evaluation of patients with rheumatic diseases. III. Comparison of serum glycoprotein, seromucoid, and C-reactive protein determinations as methods for the evaluation of patients with rheumatic fever, 510

PEARSON, HOWARD A., AND CONE, THOMAS E., JR., Anhidrotic ectodermal dysplasia with vascular purpura, 306

PICK, WALTER (WITH ROSS, FREDERICK P.), The management of hypertrophic pyloric stenosis in a community hospital, 49

PINHEIRO, DÁCIO, Tetanus, 171

PINTO, PETER S., AND KIEFER, JOSEPH N., Infarction of the testicle in the newborn infant, 80

PIZZI, TULIO (WITH ARIZTÍA, ANÍBAL, BUSTAMANTE, WERNER, MORENO, LUIS, DOBERTI, ARMANDO, ROMÁN, CLARA, AND DÍAZ, MARÍA), Interstitial plasma cell pneumonia and Pneumocystis carinii, 639

POUNDERS, CARROLL M., Proctalgia fugax infantum, 413

PRICE, RICHARD D. (WITH MUNSLOW, RALPH A., STOVALL, VIRGINIA S., AND KOHLER, COLETTE M.), Brain abscess in infants, 74

R

RAMOS-GALVÁN, RAFAEL (WITH GÓMEZ, FEDERICO, CRAVIOTO, JOAQUÍN, FRENK, SILVESTRE, DE LA PEÑA, CARMEN, MORENO, MARÍA ELENA, AND VILLA, MARÍA ELENA), Influence of L-lysine supplements on the absorption and retention of nitrogen from milk by children with protein malnutrition, 262

RICE, E. CLARENCE (WITH GILBERT, ENID F., AND GREGORY, KRIKOR, O.), Paper electrophoretic study of serum proteins in children with leukemia, 238

RICHLAN, A. (WITH SIDERIDES, L. E., AND ANTONIUS, N. A.), Unusual auricular flutter in newborn infant, 435

ROBERTS, PAUL H. (WITH NEMIR, ROSA LEE, AND BARRY-LEDEAUX, SALLY), Observations of antistreptolysin-O, C-reactive protein and electrophoretic protein patterns in maternal and neonatal sera, 493

ROBINOW, MEINHARD, Correspondence, 614

Román, Clara (with Ariztía, Aníbal, Bustamante, Werner, Moreno, Luis, Doberti, Armando, Pizzi, Tulio, and Díaz, María), Interstitial plasma cell pneumonia and Pneumocystis carinii, 639

Rosenblum, Arthur (with Matheson, A., Glazer, Richard, and Dacanay, Eleonora), Local tissue and blood eosinophils in newborn infants, 502

Ross, Frederick P., and Pick, Walter, The management of hypertrophic pyloric stenosis in a community hospital, 49

Rowe, Richard D., and James, L. S., The normal pulmonary arterial pressure during the first year of life, 1

— (with James, L. S.), The pattern of response of pulmonary and systemic arterial pressures in newborn and older infants to short periods of hypoxia, 5

Ryan, Donnalda (with Crump, E. Perry, Horton, Carrell P., and Masuoka, Jitsuichi), Growth and development. I. Relation of birth weight in Negro infants to sex, maternal age, parity, prenatal care, and socioeconomic status, 678

S

Schweinsberger, Richard A., and Muhler, Joseph C., Urinary excretion of fluoride by children aged two through five years using a stannous fluoride-containing dentifrice in a natural fluoride area and a nonfluoride area, 634

Scott, Roland B. (with Ferguson, Angella D., and Teixeira, Gertrude C.), Novobiocin in common pediatric infections, 655

Sherry, S. Norman (with Kramer, Irving), The time of passage of the first stool and urine by the premature infant, 373

Sherwood, Mildred M., Correspondence, 486

Shetlar, M. R., Payne, R. W., Strenge, Henry B., and Faulkner, Jane Bullock, Objective evaluation of patients with rheumatic diseases. III. Comparison of serum glycoprotein, seromucoid, and C-reactive protein determinations as methods for the evaluation of patients with rheumatic fever, 510

Shinaberger, James H., Tomsovic, Edward J., and Butz, William C., Fatal acute appendicitis in a fifteen-day-old infant, 422

Siderides, L. E., Antonius, N. A., and Richlan, A., Unusual auricular flutter in newborn infant, 435

Slotkowski, Eugene L., Formation of mucous membrane lesions secondary to prolonged use of one per cent aqueous gentian violet, 652

Stanley-Brown, Edward G., and Stark, Richard B., The management of facial trauma in infants and children, 285

Stark, Richard B. (with Stanley-Brown, Edward G.), The management of facial trauma in infants and children, 285

Steendijk, R. (with de Bruijne, J. I., and van Creveld, S.), Surgical treatment of pyloric stenosis in an infant with hemophilia A, 698

Stokes, Joseph, Jr., Profile of Samuel McClintock Hamill, 606

Storer, John, and Kiragus, Chahnour, Considerations on an unrecognized mediastinal cyst, 194

Stovall, Virginia S. (with Munslow, Ralph A., Price, Richard D., and Kohler, Colette M.), Brain abscess in infants, 74

Strenge, Henry B. (with Shetlar, M. R., Payne, R. W., and Faulkner, Jane Bullock), Objective evaluation of patients with rheumatic diseases. III. Comparison of serum glycoprotein, seromucoid, and C-reactive protein determinations as methods for the evaluation of patients with rheumatic fever, 510

Strominger, Donald B., James, David H., and Goldring, David, Constant infusion pump for limiting fluids, 310

T

Teixeira, Gertrude C. (with Ferguson, Angella D., and Scott, Roland B.), Novobiocin in common pediatric infections, 655

Tevetoğlu, Fethi, and Abbey, Joseph A., Chlorpromazine in pediatric surgery, 181

— (with Gardner, Joseph E.), The roentgenographic diagnosis of geophagia (dirt-eating) in children, 667

Thomas, W. A. (with Goldring, D., Behrer, M. R., McCoy, E., and O'Neal, R. M.), Clinical and pathological observations in infants with coaretation of the aorta and patent ductus arteriosus, 18

Tietz, K. George, and Davis, John B., Ruptured ovarian cyst in a newborn infant, 564

Tolmas, Hyman C., Favism, 445

Tomsovic, Edward J. (with Shinaberger, James H., and Butz, William C.), Fatal acute appendicitis in a fifteen-day-old infant, 422

Torres, Francisco E. (with Barness, Lewis A., Baker, David, Guilbert, Paul, and György, Paul), Nitrogen metabolism of infants fed human and cow's milk, 29

V

VAN CREVELD, S. (WITH DE BRUIJNE, J. I., AND STEENDIJK, R.), Surgical treatment of pyloric stenosis in an infant with hemophilia A, 698

VILLA, MARÍA ELENA (WITH GÓMEZ, FEDERICO, RAMOS-GALVÁN, RAFAEL, CRAVIOTO, JOAQUÍN, FRENK, SILVESTRE, DE LA PEÑA, CARMEN, AND MORENO, MARÍA ELENA), Influence of L-lysine supplements on the absorption and retention of nitrogen from milk by children with protein malnutrition, 262

W

WALKER, RICHARD H., Appendicitis in the newborn infant, 429

WANG, G. C. (WITH BAIN, G. O., AND MISANIK, L. F.), Giant cell hepatitis associated with hereditary spherocytosis, 549

WEBB, C. H. (WITH MCLELLAN, M. S.), Ear studies in the newborn infant, 672

WHITE, HARVEY (WITH KRAUS, MICHAEL), Congenital tracheoesophageal fistula in the neck without atresia, 580

WIENER, HARRY (WITH KOZINN, PHILIP J., AND COHEN, PHILIP), Infantile amaurotic family idiocy, 58

WIENER, JOSEPH, Septicemia of the newborn due to Listeria monocytogenes, 392

Y

YUN, DUK JIN, Infant and child mortality in a Korean rural area, 709

SUBJECT INDEX*

A

Abscess, brain, in infants (Munslow et al.), 74
Abt, Isaac, Arthur, profile of (Parmelee), 106
Adrenal hypoplasia, ectopic and hypoplastic pituitary with (Ehrlich), 377
Agenesis of spleen (Blattner), 350
Akerfeldt serum test for schizophrenia in children (Brown), 46
Amaurotic family idiocy, infantile (Kozinn et al.), 58
  juvenile (Vogt-Spielmeyer disease), three cases of, with electroencephalographic findings (Crawley), 571
Antistreptolysin-O, C-reactive protein and electrophoretic protein patterns in maternal and neonatal sera (Nemir et al.), 493
Appendicitis, fatal acute, in 15-day-old infant (Shinaberger), 422
  in newborn infant (Walker), 429
Asthma, infectious, and recurrent respiratory infections, acellular bacterial antigen complex (Hoffmann) in treatment of children with (Gundy), 516
Atrial outflow, left, obstruction to, by supravalvular stenosing ring (Johnson and Dodd), 190
Attitudes, importance of (editorial), 620
Auricular flutter, unusual, in newborn infant (Siderides et al.), 435

B

Bacitracin and penicillin ointments in ophthalmia neonatorum prophylaxis, comparison of ocular reactions using (Margileth), 646
Bacterial antigen complex, acellular (Hoffmann) in treatment of children with recurrent respiratory infections and infectious asthma (Gundy), 516
BCG vaccination against tuberculosis (Rosenthal), 229
  in Virginia (Kendig), 54
Benzathine penicillin G, comparison of intramuscular and oral, in treatment of streptococcal infections in children (Breese and Disney), 157
Blood eosinophils, local tissue and, in newborn infants (Matheson et al.), 502
Brain abscess in infants (Munslow et al.), 74
Books:
  A synopsis of children's diseases (Rendle-Short), 619
  A visit to the hospital (Chase), 229
  Ageing in transient tissues (Wolstenholme and Millar, eds.), 122
  An atlas of cardiac surgery (Rodriguez), 490
  Atlas of clinical endocrinology (Lisser and Escamillo), 122
  Blindness in children (Norris et al.), 618
  Children's eye problems (Krimsky), 358
  Chirurgie (Dubois et al.), 229
  Clinical toxicology of commercial products (Gleason et al.), 228
  Dermatologic formulary (Pascher, ed.), 750
  Diabetes mellitus, with emphasis on children and young adults (Danowski), 122
  Dorland's illustrated medical dictionary, 121
  Endocrine disorders in childhood and adolescence (Wilkins), 490
  Epilepsy (Fairfield), 618
  La puberté (Laroche, ed.), 229
  Liver, structure and function (Papper and Schaffner), 619
  Magnetic removal of foreign bodies (Equen), 750
  Modern therapy in neurology (Forster, ed.), 228
  Orthopaedic surgery in infancy and childhood (Ferguson), 358
  Pediatric dentistry (Cohen), 619
  Perinatal loss in modern obstetrics (Nesbitt), 618
  Stuttering (Hahn), 122
  The compleat pediatrician (Davison and Levinthal), 121
  The doctor as a witness (Tracy), 121
  The essentials of paediatrics for nurses (Kessel), 230
  The family book of child care (Newton), 120
  The fight for fluoridation (McNeil), 359
  The mentally ill child; a guide for parents (Getz and Rees), 617

*July, pp. 1-124; August, pp. 125-232; September, pp. 233-362; October, pp. 363-492; November, pp. 493-620; December, pp. 621-754.

Books—Cont'd
The metabolic response to neonatal surgery (Rickham), 617
The physiology and biochemistry of lactation (Folley), 490
The placement of adoptive children (Wittenborn), 749
The premature baby (Crosse), 619
The treatment of burns (Artz and Reiss), 230
The writing road to reading (Spalding), 230
Water fluoridation: facts not myths (Dublin), 359
When children ask (Bro), 120

C

Cerebral lateral dominance variations, frequency among school children of premature and full-term birth (Eames), 300
Cerebrospinal fluid glucose, low, associated with meningeal neoplasia (Dungan and McKey), 186
China, Red, medicine in (editorial), 360
Chlorpromazine in pediatric surgery (Tevetoğlu and Abbey), 181
Clinical Pathological Conferences:
hyaline membrane disease, 322
hypercalcemia, 461
intrahepatic liver disease, 584
pneumococcal sepsis after splenectomy, 716
septicemia, 85
tuberculous meningitis, 212
Coaretation of aorta and patent ductus arteriosus, clinical and pathological observations in infants with (Goldring et al.), 18
Cold injury in newborn infant (editorial), 121
Comments on Current Literature:
agenesis of spleen, 350
intrauterine fetal oxygenation, 115
mumps virus and subacute thyroiditis, 483
natural immunity to poliomyelitis, 742
recent developments in study of measles virus, 611
severe infections in splenectomized infants and children, 223
Congenital anomaly of inferior vena cava (Edwards and Bennett), 453
defect in musculature of stomach resulting in spontaneous gastric perforation in neonatal period (Meyer), 416
heart disease, early definitive diagnosis of patients with (Adams), 202
Correspondence, 116, 226, 486, 614, 745
C-Reactive protein, antistreptolysin-O, and electrophoretic protein patterns in maternal and neonatal sera (Nemir et al.), 493
serum glycoprotein, and seromucoid determinations as methods for evaluation of patients with rheumatic fever, comparison of (Shetlar et al.), 510
Cretinism, sporadic, with goiter, occurring in identical twins (Frierson et al.), 704
Cytomegalic inclusion disease, generalized (McElfresh and Arey), 146

D

Development, growth, and relation of birth weight in Negro infants to sex, maternal age, parity, prenatal care, and socioeconomic status (Crump et al.), 678
Ductus arteriosus in neonatal period (Mitchell), 12
patent, and coaretation of aorta, clinical and pathological observations in infants with (Goldring et al.), 18
early diagnosis of (Holve and Adams), 164

E

Ear studies in newborn infant (McLellan and Webb), 672
Ectodermal dysplasia, anhidrotic, with vascular purpura (Pearson and Cone), 306
Editor's Column:
a Journal of Pediatrics Fund for furthering pediatrics, 751
cold injury in newborn infant, 121
importance of attitudes, 620
is pediatric practice a satisfying lifework? 751
medicine in Red China, 360
physicians' charges and cost of living, 492
pyloric stenosis and community hospital, 122
sterilization of instruments for prevention of hepatitis, 491
"the times have changed," 231
Electrophoretic protein patterns, antistreptolysin-O, and C-reactive protein in maternal and neonatal sera (Nemir et al.), 493
study, paper, of serum proteins in children with leukemia (Gilbert et al.), 238
Emphysema, pulmonary interstitial, with air-block syndrome (Berman and Kahn), 457
Epileptic child and his parents, social management of (Livingston), 137
Esophagus of young infant, foreign body (paper clip) in (Michamin and Gonne), 197

F

Facial trauma in infants and children, management of (Stanley-Brown and Stark), 285
Familial fibrous swelling of jaws (Hogan and Liebner), 554
Favism (Tolmas), 445
Feet, children's, examination of (Miller), 527

Fetal oxygenation, intrauterine (Blattner), 115
Fluoride excretion, urinary, by children aged 2-5 years using stannous fluoride-containing dentifrice in natural fluoride area and nonfluoride area (Schweinsberger and Muhler), 634
Foreign body (paper clip) in esophagus of young infant (Nichamin and Gonne), 197
Fund, Journal of Pediatrics, for furthering pediatrics (editorial), 751

G

Gastric perforation, spontaneous, in neonatal period, congenital defect in musculature of stomach resulting in (Meyer), 416
Gentian violet, 1 per cent aqueous, formation of mucous membrane lesions secondary to prolonged use of (Slotkowski), 652
Geophagia (dirt-eating) in children, roentgenographic diagnosis of (Gardner and Tevetoğlu), 667
Giant cell hepatitis associated with hereditary spherocytosis (Bain et al.), 549
Goiter, sporadic cretinism with, occurring in identical twins (Frierson et al.), 704
Growth and development; relation of birth weight in Negro infants to sex, maternal age, parity, prenatal care, and socioeconomic status (Crump et al.), 678

H

Hamill, Samuel McClintock, profile of (Stokes), 606
Heart and lungs, changes at birth (James), 95
  disease, congenital, early definitive diagnosis of patients with (Adams), 202
Hemodialysis in children (Carter et al.), 125
Hemophilia (McElfresh), 474
  A, surgical treatment of pyloric stenosis in infant with (de Bruijne et al.), 698
Hepatitis, giant cell, associated with hereditary spherocytosis (Bain et al.), 549
  sterilization of instruments for prevention of (editorial), 491
Hyaline membrane disease (CPC), 322, (Curtis), 726
Hypercalcemia (CPC), 461
Hypertrophic pyloric stenosis, management of, in community hospital (Ross and Pick), 49
Hypoproteinemia, idiopathic (Degnan), 448
Hypoxia, pattern of response of pulmonary and systemic arterial pressures in newborn and older infants to short periods of (James and Rowe), 5

I

Identical twins, sporadic cretinism with goiter occurring in (Frierson et al.), 704
Importance of attitudes (editorial), 620
Infant and child mortality in Korean rural area (Yun), 709
  15-day-old, fatal acute appendicitis in (Shinaberger), 422
Infantile amaurotic family idiocy (Kozinn et al.), 58
Infants and children, facial trauma in, management of (Stanley-Brown and Stark), 285
  undernourished, studies on protein metabolism in (Matsaniotis), 267
  brain abscess in (Munslow et al.), 74
Inferior vena cava, anomaly of (Edwards and Bennett), 453
Infusion pump, constant, for limiting fluids (Strominger et al.), 310
Interstitial plasma cell pneumonia and Pneumocystis carinii (Ariztía et al.), 639
Intrahepatic liver disease (CPC), 584
Intrauterine fetal oxygenation (Blattner), 115

J

Jaws, familial fibrous swelling of (Hogan and Liebner), 554

K

Korean rural area, infant and child mortality in (Yun), 709

L

Lactose, effect on nitrogen metabolism and phenol excretion in infants (Cornely et al.), 40
Leiner's disease, seborrheic dermatitis of infants and, a biotin deficiency (Nisenson), 537
Leukemia, congenital, associated with mongolism (Lee and Ciner), 303
  paper electrophoretic study of serum proteins in children with (Gilbert et al.), 238
Listeria monocytogenes, septicemia in newborn due to (Wiener), 392
Liver disease, intrahepatic (CPC), 584
Lungs and heart, changes at birth (James), 95
L-Lysine supplement, influence on absorption and retention of nitrogen from milk by children with protein malnutrition (Gómez et al.), 262

M

Measles virus, recent developments in study of (Blattner), 611
Mediastinal cyst, unrecognized, considerations on (Storer and Kiragus), 194

Medical Progress:
changes in heart and lungs at birth (James), 95
hemophilia (McElfresh), 474
hyaline membrane disease (Curtis), 726
pediatrician and his changing world (Fischer), 593
progress in neuropsychiatry (Eisenberg), 334
Medicine in Red China (editorial), 360
Meningeal neoplasia, low cerebrospinal fluid glucose associated with (Dungan and McKey), 186
Meningitis, acute purulent, treatment with tetracycline (Koch and Hansen), 65
tuberculous (CPC), 212
Milk, human and cow's, nitrogen metabolism of infants fed (Barness et al.), 29
influence of L-lysine supplements on absorption and retention of nitrogen from, by children with protein malnutrition (Gómez et al.), 262
Mongolism, congenital leukemia associated with (Lee and Ciner), 303
Mortality, infant and child, in Korean rural area (Yun), 709
Mucous membrane lesions secondary to prolonged use of 1 per cent aqueous gentian violet, formation of (Slotkowski), 652
Mumps virus and subacute thyroiditis (Blattner), 483

N

Neonatal period, congenital defect in musculature of stomach resulting in spontaneous gastric perforation in (Meyer), 416
ductus arteriosus in (Mitchell), 12
Nephrotic syndrome associated with renal vein thrombosis (Feinerman et al.), 385
Neuroblastoma, roentgenographic findings associated with (Hansman and Girdany), 621
Neurofibrosarcoma, digital, in infancy (Jensen et al.), 566
Neuropsychiatry, progress in (Eisenberg), 334
Newborn and older infants, pattern of response of pulmonary and systemic arterial pressures to short periods of hypoxia (James and Rowe), 5
infant(s), appendicitis in (Walker), 429
cold, injury in (editorial), 121
ear studies in (McLellan and Webb), 672
infarction of testicle in (Pinto and Kiefer), 80
local tissue and blood eosinophils in (Matheson et al.), 502
ruptured ovarian cyst in (Tietz and Davis), 564
septicemia of, due to Listeria monocytogenes (Wiener), 392
unusual auricular flutter in (Siderides et al.), 435
News and Notes, 116, 227, 354, 488, 615, 748
Niemann-Pick disease in boy of 16 months (Pansky and Lee), 290
Nitrogen absorption and retention from milk by children with protein malnutrition, influence of L-lysine supplements on (Gómez et al.), 262
metabolism and phenol excretion in infants, effect of lactose on (Cornely et al.), 40
of infants fed human and cow's milk (Barness et al.), 29
Novobiocin, apparent sensitization to (Hughes), 664
in common pediatric infections (Ferguson et al.), 655

O

Ocular reactions, comparison of, using penicillin and bacitracin ointments in ophthalmia neonatorum prophylaxis (Margileth), 646
Ophthalmia neonatorum prophylaxis, comparison of ocular reactions using penicillin and bacitracin ointments in (Margileth), 646
Ovarian cyst, ruptured, in newborn infant (Tietz and Davis), 564
Oxygenation, fetal, intrauterine (Blattner), 115

P

Pediatric practice, is it a satisfying lifework? (editorial), 751
Pediatric Profiles:
Isaac Arthur Abt (Parmelee), 106
Samuel McClintock Hamill (Stokes), 606
Pediatric rewards (Parmelee) (editorial), 752
Pediatrician and his changing world (Fischer), 593
Penicillin and bacitracin ointments in ophthalmia neonatorum prophylaxis, comparison of ocular reactions using (Margileth), 646
G, benzathine, comparison of intramuscular and oral, in treatment of streptococcal infections in children (Breese and Disney), 157
Phenol excretion and nitrogen metabolism in infants, effect of lactose on (Cornely et al.), 40
Physicians' charges and cost of living (editorial), 492
Pituitary, ectopic and hypoplastic, with adrenal hypoplasia (Ehrlich), 377
Pneumococcal sepsis after splenectomy (CPC), 716
Pneumocystis carinii, interstitial plasma cell pneumonia and (Ariztía et al.), 639
Poliomyelitis, natural immunity to (Blattner), 742
transplacental transmission of (Barsky and Beale), 207

Premature and full-term birth, school children of, frequency of cerebral lateral dominance variations among (Eames), 300
infant, time of passage of first stool and urine by (Kramer and Sherry), 373
Proctalgia fugax infantum (Pounders), 413
Protein malnutrition, influence of L-lysine supplements on absorption and retention of nitrogen from milk by children with (Gómez et al.), 262
metabolism in undernourished infants and children, studies on (Matsaniotis), 267
Pulmonary and systemic arterial pressures in newborn and older infants, pattern of response of, to short periods of hypoxia (James and Rowe), 5
arterial pressure, normal, during first year of life (Rowe and James), 1
interstitial emphysema with air-block syndrome (Berman and Kahn), 457
Purpura, vascular, anhidrotic ectodermal dysplasia with (Pearson and Cone), 306
Purulent meningitis, acute, treatment with tetracycline (Koch and Hansen), 65
Pyloric stenosis and community hospital (editorial), 122
hypertrophic, management of, in community hospital (Ross and Pick), 49
in infant with hemophilia A, surgical treatment of (de Bruijne et al.), 698

R

Renal vein thrombosis, nephrotic syndrome associated with (Feinerman et al.), 385
Respiratory infections, recurrent, and infectious asthma, acellular bacterial antigen complex (Hoffmann) in treatment of children with (Gundy), 516
Rheumatic fever, comparison of serum glycoprotein, seromucoid, and C-reactive protein determinations as methods for evaluation of patients with (Shetlar et al.), 510
steroid therapy for (McCue), 255
Russia, child care in (Bakwin), 313

S

Schizophrenin in children, serum Akerfeldt test for (Brown), 46
Seborrheic dermatitis of infants and Leiner's disease, a biotin deficiency (Nisenson), 537
Sensitization, apparent, to novobiocin (Hughes), 664
Septicemia (CPC), 85
of newborn due to Listeria monocytogenes (Wiener), 392
Seromucoid, serum glycoprotein, and C-reactive protein determinations as methods for evaluation of patients with rheumatic fever, comparison of (Shetlar et al.), 510
Serum glycoprotein, seromucoid, and C-reactive protein determinations as methods for evaluation of patients with rheumatic fever, comparison of (Shetlar et al.), 510
proteins in children with leukemia, paper electrophoretic study of (Gilbert et al.), 238
Spleen, agenesis of (Blattner), 350
Splenectomized infants and children, severe infections in (Blattner), 223
Splenectomy, pneumococcal sepsis after (CPC), 716
Sterilization of instruments for prevention of hepatitis (editorial), 491
Steroid therapy for rheumatic fever (McCue), 255
Stomach, congenital defect in musculature of, resulting in spontaneous gastric perforation in neonatal period (Meyer), 416
Stool, first, and urine, time of passage by premature infant (Kramer and Sherry), 373
Streptococcal infections in children, comparison of intramuscular and oral benzathine penicillin G in treatment of (Breese and Disney), 157
Sulfhemoglobinemia, congenital (Miller), 233

T

Testicle, infarction of, in newborn infant (Pinto and Kiefer), 80
Tetanus (Pinheiro), 171
Tetracycline, treatment of acute purulent meningitis with (Koch and Hansen), 65
Thyroiditis, subacute, mumps virus and (Blattner), 483
"Times have changed" (editorial), 231
Tracheoesophageal fistula in neck, congenital, without atresia (Kraus and White), 580
Transplacental transmission of poliomyelitis (Barsky and Beale), 207
Tuberculous meningitis (CPC), 212
Tularemia, oropharyngeal (Hughes and Etteldorf), 363

U

Urinary calculus disease among Israeli immigrant and Arab children (Levy and Falk), 404

V

Vaccination, BCG, in Virginia (Kendig), 54
Vena cava, inferior, anomaly of (Edwards and Bennett), 453

INDEX NUMBER

Hospital Library

Vol. 51 DECEMBER, 1957 No. 6

THE UNIVERSITY OF MICHIGAN
APR 16 1959
MEDICAL LIBRARY

THE JOURNAL OF PEDIATRICS

A MONTHLY JOURNAL DEVOTED TO THE PROBLEMS AND DISEASES OF INFANCY AND CHILDHOOD

Editor
BORDEN S. VEEDER
St. Louis

Editorial Board

HARRY BAKWIN	New York
RUSSELL J. BLATTNER	Houston
A. LAWRENCE CHUTE	Toronto
STEWART H. CLIFFORD	Boston
JAMES N. ETTELDORF	Memphis
ALEXIS F. HARTMANN	St. Louis
LEE FORREST HILL	Des Moines
WALDO E. NELSON	Philadelphia
CARL H. SMITH	New York

Contributing Editors

ERNEST CAULFIELD	West Hartford
SIDNEY FARBER	Boston

PUBLISHED BY THE C. V. MOSBY COMPANY, 3207 WASHINGTON BLVD., ST. LOUIS 3, U. S. A.
Copyright © 1957 by The C. V. Mosby Company

Table of Contents on 3rd Cover

for the first few days of life

VI-PENTA #1

provides K, E, and C, the vitamins needed particularly by prematures and newborns.

for infants and young children

VI-PENTA #2

provides vitamins A, D, C, and E, essential for normal development.

for all ages

VI-PENTA #3

provides A, D, C, and 5 B-complex vitamins for the greater nutritional demands of the growing years.

Identical in content and taste to the long-established VI-Penta® Drops.

FOR PROGRESSIVE VITAMIN THERAPY

ROCHE LABORATORIES • Division of Hoffmann-La Roche Inc. • Nutley 10, N. J.

Vol. 51, No. 6, December, 1957. The Journal of Pediatrics is published monthly by The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Mo. Subscription rates: United States and its Possessions $12.00, Students $6.00; Canada, Latin-America, and Spain $13.00, Students $7.00; Other Countries $14.00, Students $8.00. Single copies $2.00 postpaid. Entered as Second-class matter June 29, 1932, at the Post Office at St. Louis, Missouri, under Act of March 3, 1879. Printed in the U. S. A.

for such manifestations of anxiety in children as **bed-wetting, sleep problems, infantile colic, irritability, moodiness, hypertonicity, poor eating...**

try **Serpasil® Elixir**

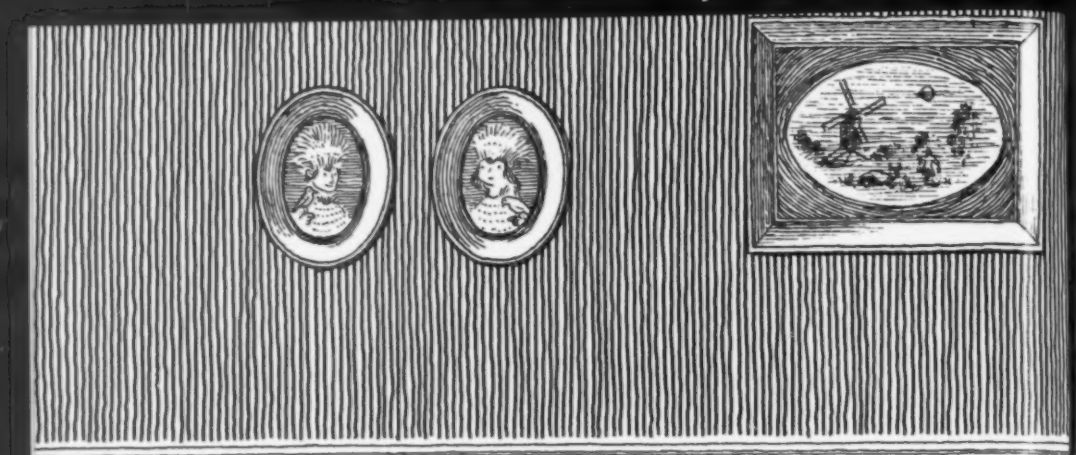
(reserpine CIBA)

Serpasil provides a shield against stress in the over-reactive, the tense, the problem child. Striking remissions have been observed in children with excessive crying, poor eating and sleeping patterns, infantile colic, and bed-wetting.

CIBA
SUMMIT, N. J.

Supplied: Elixir, 1 mg. and 0.2 mg. Serpasil per 4-ml. teaspoon.

2/2397MK



they've heard the call for Vi-Daylin®

Each delicious, 5-cc. teaspoonful of Vi-Daylin contains:

Vitamin A	0.9 mg. (3000 units)
Vitamin D	20 mcg. (800 units)
Thiamine Hydrochloride	1.5 mg.
Riboflavin	1.2 mg.
Pyridoxine Hydrochloride	1 mg.
Ascorbic Acid	40 mg.
Vitamin B_{12}	3 mcg.
Nicotinamide	10 mg.

Abbott

712203

ERIK BLEGVAD·ST

kids' coughs and coughing kids

respond to drop-dosage

DIATUSSIN®

non-narcotic cough control

When coughs harass the child—and his mother—a few drops of DIATUSSIN lessen both frequency and severity of cough... without sedating or upsetting the youngster.

Even medication-shy children just naturally take to drop-dosage DIATUSSIN, either on food, in drink or dropped directly on the tongue.

Dosage: *Children under 5 years*...2 to 4 drops, 3 or 4 times daily. *Over 5 years*...5 drops, 3 or 4 times daily. *Severe cases*...2 drops every 2 or 3 hours. *Adults*...up to 7 drops, 3 or 4 times daily.

Formula: Extracts of Thyme and Drosera in an alcoholic menstruum (alcohol content 22%).

Supplied in 6-cc. bottles with plastic dropper.

Also available: DIATUSSIN Syrup (containing 2 drops of extract per teaspoonful) in 4-oz., pint and gallon bottles.

AMES COMPANY, INC · ELKHART, INDIANA

Ames Company of Canada, Ltd., Toronto

24057

kids put aside their blocks for

PALADAC®

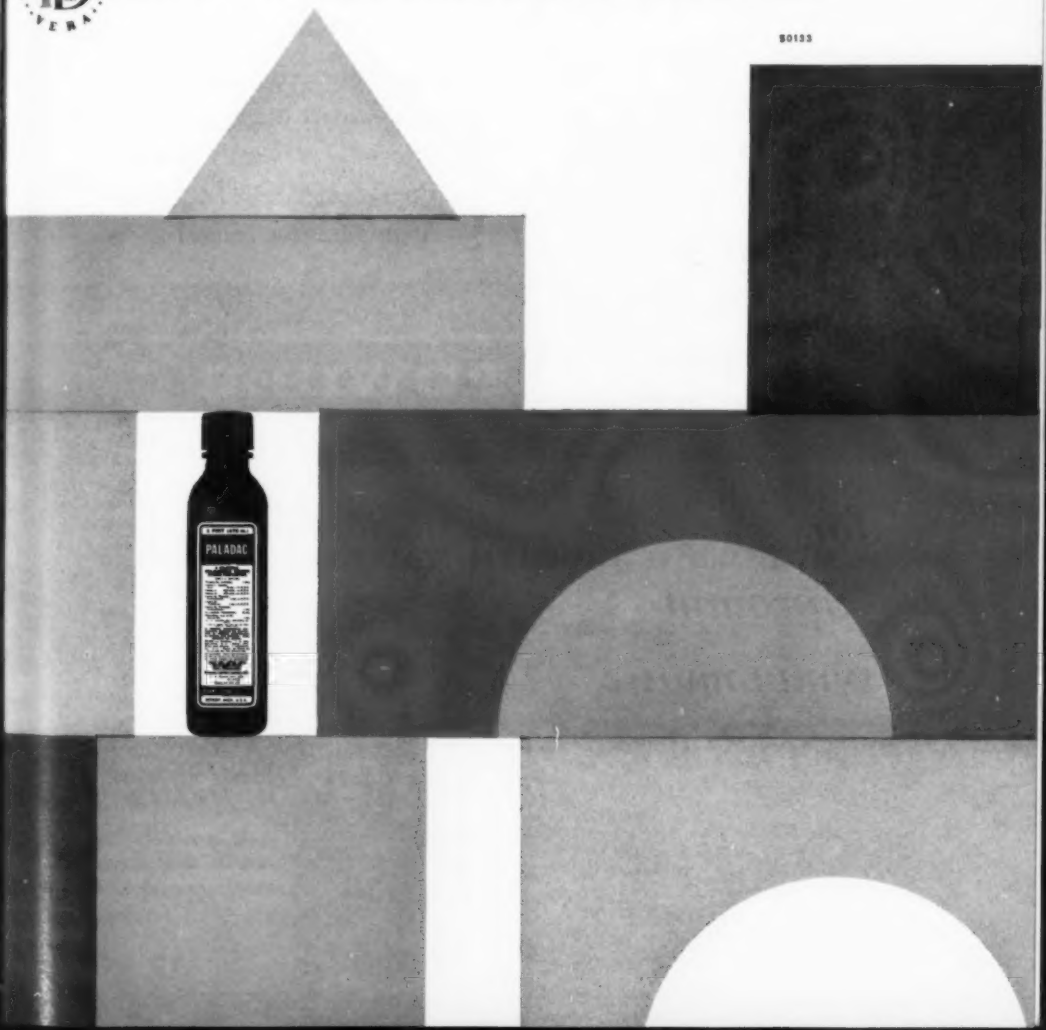
liquid multivitamin supplement

Its appealing orange color, aroma and flavor make PALADAC a universal favorite with children...and its balanced nine-vitamin formula amply supplements their diet.

PALADAC is even-flowing; readily miscible, if desired, with milk, fruit juice or other foods; and requires no refrigeration. Available in 4-ounce and 16-ounce bottles.

PARKE, DAVIS & COMPANY • DETROIT 32, MICHIGAN

B0133



now 2

palatable

and effective

antidiarrheals

containing

Carob powder buffers intestinal contents and adsorbs irritant secretions, bacteria, and toxins. Its marked demulcent properties check hyperperistalsis, permitting fluid absorption and rapidly producing formed stools. Carob powder tends to prevent dehydration and loss of electrolytes and the patient can usually be maintained on adequate nutritious diets during treatment.

The high soluble carbohydrate content (mainly fructose) of carob powder provides valuable nutritional support and tends to counteract *diarrhea-induced acidosis.*

CAROB POWDER

for

prompt

symptomatic

control

PITMAN-MOORE COMPANY

DIVISION OF
ALLIED LABORATORIES, INC.
INDIANAPOLIS 6, INDIANA

Carob powder with streptomycin/neomycin

INTROMYCIN™

Carob Powder . . . for prompt relief of diarrhea symptoms

Neomycin/Streptomycin... for the prevention and treatment of bacterial infections

your patients recover more rapidly with **INTROMYCIN**

because

- formed stools are produced 5 times faster[1]
- water loss is better controlled
- electrolytes are replenished
- bacterial pathogens are inhibited

1. Abella, P.U.: J. Pediat. 41:82, 1952.

Available in 75 Gram (2½ oz.) bottles.

Have you taken the **INTROMYCIN** *taste test?*

Carob powder without antibiotics

AROBON®

Arobon alone controls most nonspecific, uncomplicated diarrheas by physiologic means—without the use of sedatives or narcotics. In infectious diarrheas, it controls the distressing symptoms when used in conjunction with appropriate antibiotic or chemotherapeutic treatment.

Originally introduced as an outstanding antidiarrheal for infants and children, Arobon has proved remarkably efficacious in the treatment of diarrheas of all age groups.

Distributed by Pitman-Moore Company under the trade name AROBON through rights acquired from the trademark owner, the Nestlé Company, Inc.

Available in 5 oz. bottles.

5 reasons why

"CYTOFERIN"®

is the logical combination in

iron deficiency anemias

"Cytoferin" combines vitamin C and ferrous iron to provide the direct approach to greater iron absorption and utilization because:

1. Iron is absorbed only in the reduced ferrous form.
2. Ingested iron can be maintained in a reduced state only in an acid environment.
3. Vitamin C given with iron acts as an acidifying and reducing agent at the site of maximum absorption.
4. Vitamin C increases the availability of iron for hemoglobin and red blood cell formation, as well as to build body reserves.
5. The combination of iron and vitamin C is likely to be better tolerated than iron alone.

"Cytoferin" Tablets—No. 705, bottles of 100 and 1,000. "Cytoferin" Liquid — No. 945, bottles of 8 fluidounces. Stable liquid preparation; non-alcoholic; extremely palatable; may be taken undiluted.

Each tablet or 10 cc. (2 tsp.) contains:

Ferrous sulfate* (3 gr.)	200 mg.
Vitamin C (ascorbic acid)	150 mg.

*Exsiccated in the tablets, and U. S. P. in the liquid.

Suggested dosages: To be taken preferably with meals. Adults and children: 1 tablet or 2 teaspoonfuls (10 cc.) two or three times daily. Infants and children: 1 teaspoonful (5 cc.) two or three times daily depending on age.

Ayerst®

Bibliography available on request.

AYERST LABORATORIES • NEW YORK, N. Y. • MONTREAL, CANADA

5714

a standard of excellence in pediatric care

Johnson & Johnson

"... unusually satisfactory in the routine care of the skin of infants ... prophylactically effective in minimizing the incidence of diaper rash and miliaria."*

*Glaser, J.; Thompson, M. L., and Benson, T. D.: A.M.A. Am. J. Dis. Child. 81:329, 1951.

Johnson's BABY LOTION

does more!

cleanses · lubricates · soothes and combats infections

Unlike many other lotions, Johnson's Baby Lotion forms a discontinuous protective oil film—not an impenetrable barrier. It contains hexachlorophene (0.5 per cent)—for potent, persistent bacteriostatic-bactericidal action. Routine use minimizes irritations—betters skin care.

nonirritating Johnson's Baby Lotion is a bland, nontoxic oil-in-water emulsion of specially compounded, pure mineral oil with lanolin. Has a neutral pH, is free from irritating hydrocarbons, contains no antioxidants or preservatives.

lets skin function normally Forms a meshwork of homogeneously dispersed, micron-sized oil droplets. This discontinuous film lets air reach the skin, permits normal heat radiation, allows perspiration to escape readily. Combats miliaria, other irritations.

combats infections Low surface tension of water-miscible lotion base permits antiseptic agent to come into close contact with the skin, rapidly control surface infections.

provides long-lasting protection Discontinuous film does not disappear readily—gives prolonged protection from irritants.

Antiseptic gives long-lasting protection from common skin contaminants.

cleanses and lubricates thoroughly Water-miscible, removes foreign matter soluble in either oil or water. Optimal oil content gives excellent lubrication and spreads smoothly.

bettering baby care through specialized research

BABY PRODUCTS DIVISION

Johnson & Johnson

IN TREATMENT OF PINWORMS

break the reinfestation cycle rectally

GENTIAN-EV

SUPPRETTES®

SUCCESSOR TO THE SUPPOSITORY

97% CURES

Within 14-28 days, virtually a 100% cure of pinworms can be obtained with combined oral medication and Gentian-Ev Supprettes rectally.[1]

THE "NEOCERA" BASE

Contains no oils or fatty materials. Consists of water-soluble Carbowaxes* with active dispersal agent.

*Trademark U.C.C.

1. Allen, F. P., Jr.: J. Ped. 46: 155, 1955.

Composition: Each Gentian-Ev Supprette contains gentian violet 0.25% and benzocaine 2.0%, in "Neocera" dispersal base.

Supplied: In jars of 14 (one complete treatment).

NO REFRIGERATION NECESSARY
Samples on Request

NEW
TWO-PHASE ATTACK

RECTALLY—Gentian-Ev Supprettes

- Break reinfestation cycle
- Kill gravid females in rectal region
- Arrest perianal itching, scratching

ORALLY—Oxyuricidal Medication

- Destroys young and adult oxyuricides in intestinal tract

GENTIAN-EV SUPPRETTES

RECTAL MANAGEMENT OF ENTEROBIUS VERMICULARIS

Webster **THE WILLIAM A. WEBSTER COMPANY, MEMPHIS 5, TENNESSEE**

Kanana Banana Flakes for *instant* mashed banana in daily routine feeding!

• PURE • PERFECTLY RIPE
• FULLY NUTRITIOUS

The addition of three parts water or milk will INSTANTLY provide the wholly-nutritious mashed banana you prescribe.

When you prescribe banana, write "Kanana"!

Kanana Banana Flakes (NOT A POWDER)

FREE SAMPLE! Fill out and mail TODAY! For content analysis and free sample, send to:

Kannengiesser & Co., 76 Ninth Ave., New York 11, N. Y.

NAME

STREET

CITY ZONE STATE

KANNENGIESSER & COMPANY, 76 NINTH AVE., NEW YORK 11, NEW YORK. In Canada: Laurentian Agencies, Ltd., 429 St. Jean Baptiste Street, Montreal, Canada

Recent Observations

On Self-Regulated Schedules For Infants

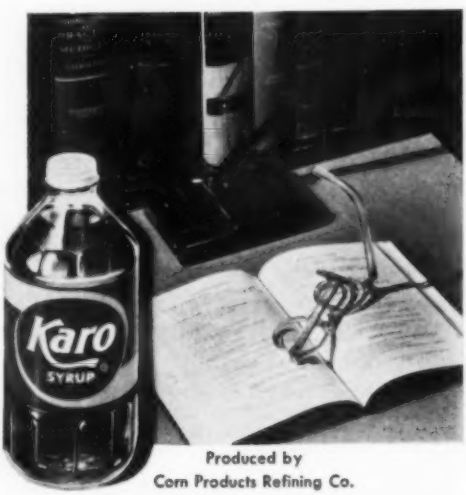
Genetically acquired behavioral predispositions enable the normal baby to regulate its feeding intake and periodic hunger sensations, its feeding habits. These physiological regulatory forces may be satisfied by adapting the formula content and feeding period to the individual needs of the infant. It involves a sensible compromise between too rigid a schedule, geared to the clock and too lax a schedule, based on self-demand feedings. Such is the current objective: for either extreme can lead to infant feeding difficulties.

The newborn may become a feeding problem if the prescribed formula is excessive or the feeding schedule rigid. Every time he is awakened abruptly from satisfying slumber to be fed forcefully, the baby gradually loses his enthusiasm for the food and begins to resist the feeding. The young infant may balk at the crude introduction of a new food or feeding procedure without the proper prelude of gradual adaptation of taste, color, consistency and quantity.

The older infant weaned from bottle to cup may reject milk or go on a hunger strike. Devoted to his bottle he resents its sudden deprivation. It takes a certain readiness for weaning to make that change agreeable. Later the infant becomes somewhat independent of his mother and arbitrary with his food. What he enjoyed yesterday, he rejects today. If he distorts the diet for a day and his mother resorts to force, a feeding problem is in the making. Sensible decorum will solve these little difficulties before they become big behavior disturbances in childhood.

The problems of infant feeding are always the same but solutions may differ with each era. The carbohydrate requirement for all infants is as completely fulfilled by KARO® Syrup today as a generation ago. Whatever the type of milk adapted to the individual infant, KARO may be added confidently because it is a balanced mixture of low sugars, easily mixed, well tolerated, palatable, hypoallergenic, resistant to fermentation, easily digestible, readily absorbed, nonlaxative. Readily available in all food stores.

MEDICAL DIVISION
CORN PRODUCTS REFINING CO.
17 Battery Place, New York 4, N.Y.



Produced by
Corn Products Refining Co.

Behind Every Karo Bottle . . . A Generation of World Literature

in diaper rash...

effective ORAL *therapy!*

effective . . . A series of 500 cases of diaper dermatitis[1] was treated—with cure resulting in all but three infants. Wherever erythematous, intertriginous zones developed in the diaper region accompanied by the pungent odor of ammonia, treatment was instituted. Ammoniacal odor disappeared with gradual relief of symptoms. As a control, 50 healthy, normal infants were given prophylactic treatment. None developed ammonia dermatitis. PEDAMETH promises effective therapy!

safe . . . dl-Methionine is safe since it is actually one of the nutritionally essential amino acids. New and Non-Official Remedies (1952) states, "Because Methionine is low in toxicity, its use is not likely to be attended by any untoward effects". Goldstein[1] states that "untoward effects were conspicuously absent". PEDAMETH promises safe therapy!

convenient . . . Simply open a capsule and add the contents to the baby's daily formula, preferably while it is still warm. Or if preferred, it may be given in fruit juice or water. But no matter how it is given—PEDAMETH is convenient therapy!

1. Goldstein, Louis S., Clinical Medicine *59*:455 (1952).

Each capsule contains 0.2 Gm. of dl-Methionine

Prescribe

PEDAMETH

(*dl·methionine* **DURST**)

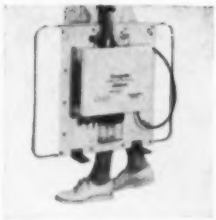
S·F·DURST & COMPANY·INC·
Philadelphia 20·Pa.

Send for samples and literature

Canadian Distributors: WINLEY-MORRIS CO., Ltd., Montreal, Quebec

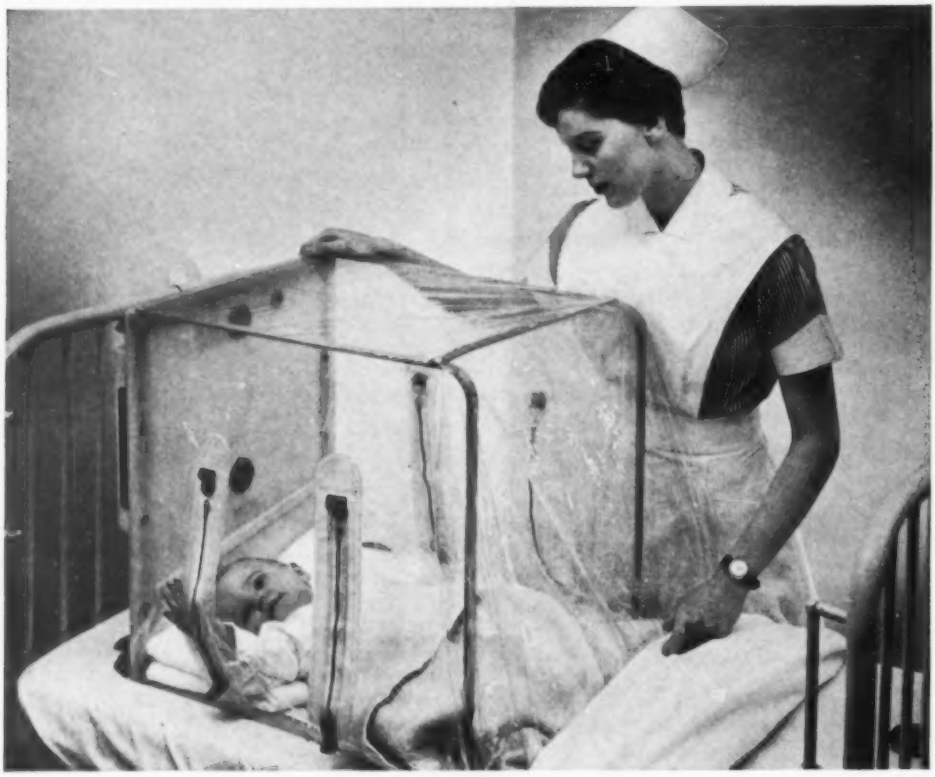
No wonder it's standard equipment

The CROUPETTE® is standard equipment in about 3,000 hospitals and 96 per cent of U. S. medical schools. First "cool vapor" croup tent, the CROUPETTE consistently excels all others in comfort, convenience and safety. The fresh, moisture-saturated air is effectively cooled and oxygenated by exclusive CROUPETTE forced circulation. Aerosol or oxygen therapy may be easily administered. With no moving parts, the CROUPETTE is as simple as it is safe and efficient.



Light, compact, portable. Includes spare atomizer.

Visibility and accessibility are CROUPETTE features. Cooled, supersaturated, aerated vapor provides immediate relief and comfort.



The **Croupette®**

Cool-Vapor and Oxygen Tent By **AIR-SHIELDS, INC.** *Hatboro, Pa. OSborne 5-5200*

For information or orders, call us collect from any point in the U.S.A.

"If I didn't hide it, he'd finish up the whole prescription at once."

"And see how he eats! See how much better he looks!"

That's the story. 'Trophite'—the high potency combination of B_{12} and B_1—is so delicious that children actually beg for more. They keep on taking it week after week, month after month—for as long as is necessary.

As a result, in a one-year controlled study of children with secondary growth failure or clinical malnutrition, Trophite's B_{12} and B_1 dramatically improved appetite and thereby increased weight and height (J. Pediat. *46*:671, 1955).

'Trophite' is available as a delicious liquid and also in convenient tablet form. Each teaspoonful (5 cc.) or tablet supplies 25 mcg. B_{12}, 10 mg. B_1.

Trophite* for appetite

high potency combination of B_{12} & B_1

Smith, Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off.

for a quick comeback

NEW V-CILLIN Drops

(Penicillin V, Lilly)

— easy way to give 'V-Cillin' to young patients

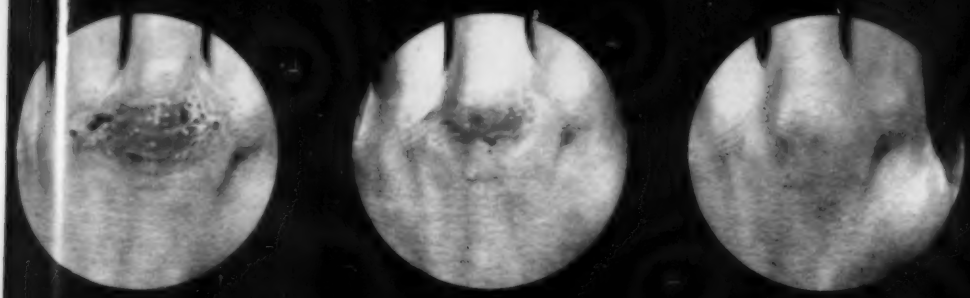
A full dose of 125 mg. (200,000 units) is administered in only 0.6 cc. The accompanying plastic dropper is safe and is designed so that mother or nurse can easily measure the dose. Pleasant mixed-fruit flavor assures patient acceptance.

Supplied in bottles of 1.5 Gm. with dropper calibrated at 125 mg. (200,000 units).

The antibiotic effectiveness of 'V-Cillin' is unsurpassed for eradicating many common infections. Its bactericidal action is particularly preferred in pediatric patients.

ELI LILLY AND COMPANY • INDIANAPOLIS 6, INDIANA, U. S. A.

733185



you can clear topical infections promptly with **NEO-POLYCIN**

...because NEO-POLYCIN provides three preferred topical antibiotics

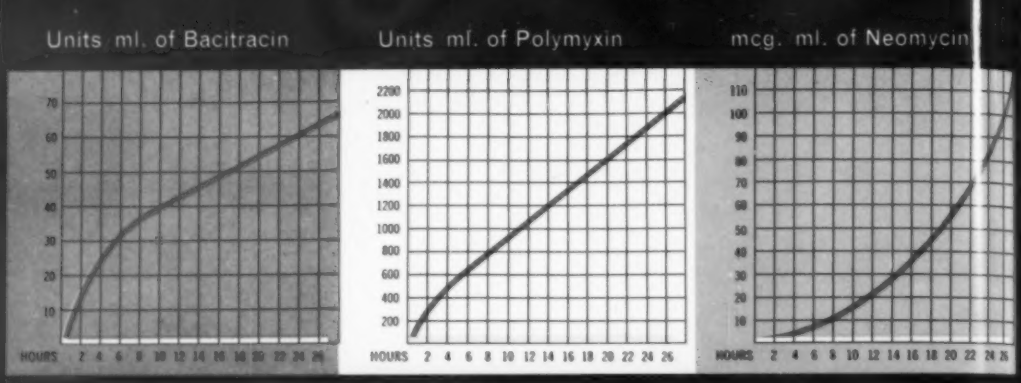
NEOMYCIN
BACITRACIN
POLYMYXIN

in a unique base which releases greater antibiotic concentrations than ordinary grease-base ointments

†Effective against the entire range of bacteria found most often in topical lesions. Proved by clinical use in pyoderma, folliculitis, paronychia, sycosis barbae, impetigo; also in secondary bacterial infections complicating treatment of burns, eczemas, contact dermatitis, seborrhea, acne, psoriasis, varicose ulcers and neurodermatitis.

PITMAN-MOORE COMPANY

...increased antibiotic concentrations for greater effectiveness in topical lesions



—antibiotics released from NEO-POLYCIN's special base.

—antibiotics released from grease-base ointment.

NEO-POLYCIN's unique **Fuzene** base permits maximal diffusion of its antibiotic content, and a higher antibiotic concentration at the site of infection than is possible with conventional grease-bases, which can release only a small fraction of their contained antibiotics. The above graphs indicate the relative amounts of neomycin, polymyxin, and bacitracin made available to the tissues from Neo-Polycin's special base and from an ordinary grease-base ointment.

NEO-POLYCIN*

(polymyxin-bacitracin-neomycin ointment)

covers the entire range of bacteria most often found in topical lesions

- **low index of sensitivity**
- **no appreciable absorption and little danger of systemic toxicity**
- **nonirritating to tissue**
- **active in presence of blood and pus**
- **diffuses readily into exudates**

*Trademark

Each gram of Neo-Polycin Ointment contains 3 mg. of neomycin, 8000 units of polymyxin B sulfate and 400 units of bacitracin in the unique Fuzene base. Supplied in 15 Gm. tubes. (Also supplied as Neo Polycin-HC, containing 1% hydrocortisone acetate, in 5 Gm. tubes.)

Neo-Polycin and Neo Polycin-HC ophthalmic ointments (anhydrous, lanolin-petrolatum base) are supplied in ⅛ oz. tubes.

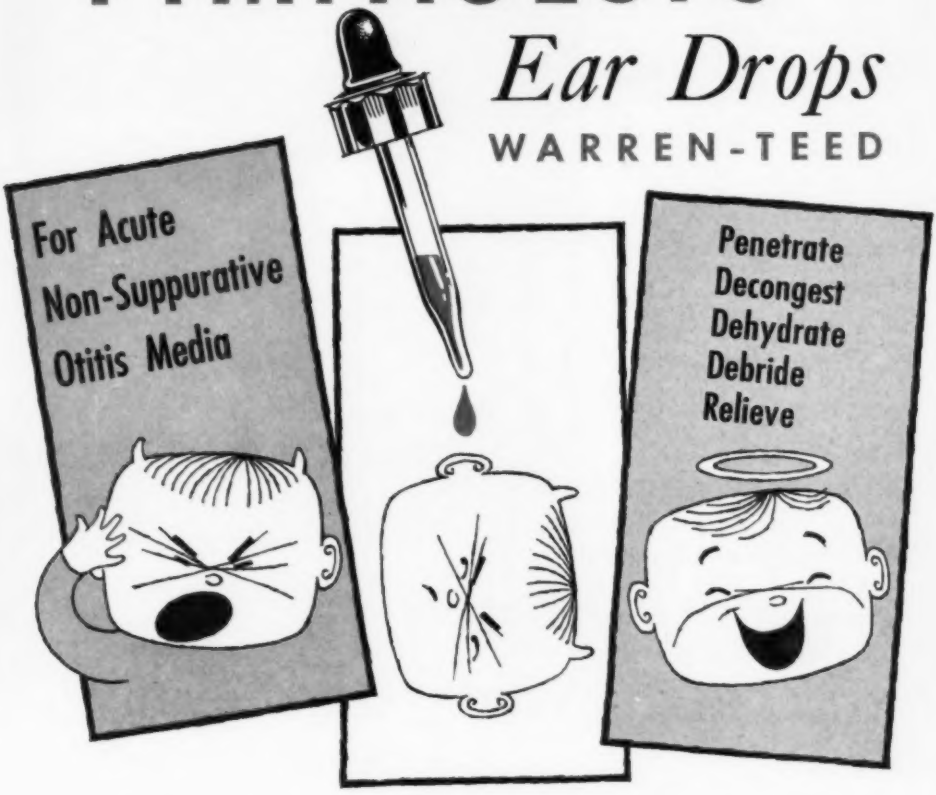
PITMAN-MOORE COMPANY

DIVISION OF ALLIED LABORATORIES, INC. • INDIANAPOLIS 6, INDIANA

TYMPAGESIC

Ear Drops

WARREN-TEED



- The penetrating, dissolving, and drying actions of its propylene glycol are far superior to those of glycerine. Phenylephrine — its positive acting decongestant — reduces swelling and discomfort. Benzocaine and antipyrine bring prompt analgesic relief from pain. Moreover, Tympagesic is safe, non-irritating, non-allergenic.

Phenylephrine Chloride	0.25%
Antipyrine	5%
Benzocaine	5%
Sodium Metabisulfite	0.1%
in Propylene Glycol	

Supplied in half-ounce dropper bottles, upon prescription.

THE WARREN-TEED PRODUCTS COMPANY
COLUMBUS 8, OHIO

WARREN-TEED *Pharmaceuticals*

CHATTANOOGA DALLAS LOS ANGELES PORTLAND

"MOTHER"
by A. Lewin-Funke

Courtesy of
The Metropolitan Museum of Art

Classic therapy
for preventing and healing
diaper rash
excoriation, chafing, irritation

DESITIN®
OINTMENT

. . . enduring in its efficacy
. . . pleasing in its simplicity
. . . exemplifying pharmaceutical elegance

SAMPLES on request **DESITIN CHEMICAL COMPANY**
812 Branch Ave., Providence 4, R. I.

any youngster with a cold or rhinitis

will appreciate the

"Novahistine effect"

When a youngster stops sniffling and begins to breathe freely in a matter of minutes...with all air passages clear and no sense of jitteriness or nasal irritation...he is experiencing the "Novahistine Effect."

THIS EFFECT IS PRODUCED BY

fast...effective decongestion

...combined with antihistaminic therapy for synergistic action

fuller utilization of medication through systemic action

...on all mucous membranes of the respiratory tract

safe, easy-to-use...ORAL dosage

unplug that stuffed-up nose orally with

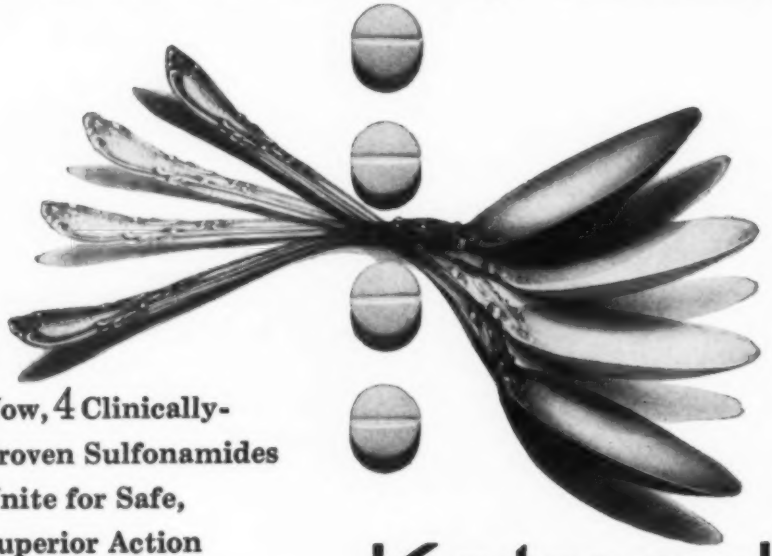
Novahistine® ELIXIR

Each 5 cc. teaspoonful provides 5.0 mg. of phenylephrine HCl and 12.5 mg. prophenpyridamine maleate.

Novahistine Elixir tastes good and solves the "nose-drop" problem with youngsters.

PITMAN-MOORE COMPANY
DIVISION OF ALLIED LABORATORIES, INC.
INDIANAPOLIS 6, INDIANA

Pluralizes Potency 4 Times!



Now, 4 Clinically-Proven Sulfonamides Unite for Safe, Superior Action

Katrasul

Chimedic

By combining 4 powerful sulfas in one palatable preparation, Katrasul provides a broad-spectrum of activity 4 times as potent as any single sulfa—with toxicity reduced to practically zero.

Katrasul's quadruple formula includes Sulfadiazine, Sulfamerazine, Sulfamethazine and Sulfacetamide—individually notable for antibacterial action—in combination exerting a 4-way antibacterial spectrum of unmatched efficacy and power.

Using only fractional dosage of each sulfa results in greater solubility and the virtual elimination of crystalluria. Sensitization reactions and toxic effects approach zero.

Prescribe Katrasul to combat both gram positive and gram negative bacilli. It is effective not only against the common microorganisms, but also the gonococcus, meningococcus, pneumococcus, staphylococcus and streptococcus infections.

Delightful coconut-custard flavor invites patient- acceptance.

•

Prompt action, safety, and pleasant taste make Katrasul highly useful in the treatment of children's infectious diseases.

•

Available: Delicious coconut-custard flavored suspension. 4oz., pints, gallons. Also in tablets.

CHICAGO PHARMACAL COMPANY

5547 N. Ravenswood Ave., Chicago 40, Illinois

Pacific Coast Branch

381 Eleventh St., San Francisco, Calif.

Nothing is
quicker...

Nothing is
more effective...

In Asthma

MEDIHALER-EPI®

Epinephrine bitartrate 7.0 mg. per cc., suspended in inert, nontoxic aerosol vehicle. Contains no alcohol. Each measured dose 0.15 mg. actual epinephrine.

For quick relief of bronchospasm of any origin. Acts more rapidly than subcutaneous epinephrine in acute allergic reactions.

THE MEDIHALER PRINCIPLE
Automatically measured-dose aerosol medications. In spillproof, leakproof, shatterproof, vest-pocket size dispensers. Also available in Medihaler-Phen™ (phenylephrine-phenylpropanolamine-hydrocortisone-neomycin) for prompt, lasting relief of nasal congestion.

MEDIHALER-ISO®

Isoproterenol sulfate 2.0 mg. per cc., suspended in inert, nontoxic aerosol vehicle. Contains no alcohol. Each measured dose 0.06 mg. actual isoproterenol.

Unsurpassed for rapid relief in asthma, bronchiectasis, emphysema.

Prescribe Medihaler medication with Oral Adapter on first prescription. Refills available without Oral Adapter.

Riker LOS ANGELES

FROM EVERY ANGLE THE

New Penn "600"

INCUBATOR of CHOICE

Infant Care...

Temperature...

Humidity...

Oxygen...

Provides a constant heat level throughout the infant compartment with accurate high humidity control . . . plus unusually convenient facilities for infant care.

Write Dept. SN-9

AMERICAN STERILIZER

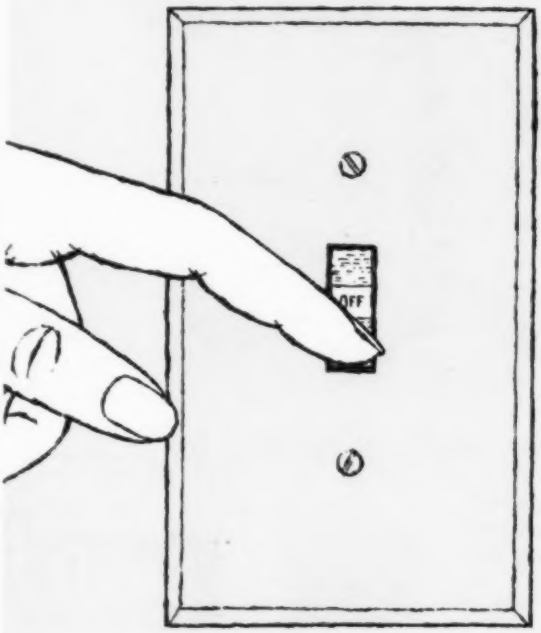
Erie · Pennsylvania

at last...

YOU CAN TURN OFF THE COUGH UNTIL MORNING...

TUSSIONEX™

A 'Strasionic' Release Product • Dihydrocodeinone Resin—Phenyltoloxamine Resin



A SINGLE DOSE GIVES 8-12 HOUR CONTROL

through sustained 'Strasionic' release.

Suppresses nighttime sleep-robbing, daytime distracting, useless coughs without interfering with the protective cough mechanism.

Over 12,000 clinical observations [1, 2, 3, 4] demonstrate its wide field of usefulness in ages ranging from 3 months to more than 70 years.

REFERENCES

(1) Chan, Y. T. and Hays, E. E., The American Journal of the Medical Sciences, August 1957; (2) Townsend, E. H., Jr., In Press; (3) Weismiller, F., In Press; (4) Cass, Leo J. and Frederik, W. S., In Press.

Now Available on Your Prescription

EACH TUSSIONEX TABLET CONTAINS:
5 mg. Dihydrocodeinone as a resin complex
10 mg. Phenyltoloxamine as a resin complex
Stock bottle of 100

EACH TEASPOON (5cc) TUSSIONEX LIQUID CONTAINS:
5 mg. Dihydrocodeinone as a resin complex
10 mg. Phenyltoloxamine as a resin complex
Stock bottle of 16 oz.

SUGGESTED DOSE: One tablet or teaspoon (5cc) q12h. Rx only. Class B taxable narcotic.

STRASENBURGH
Originators of 'Strasionic' (sustained ionic) release

R. J. STRASENBURGH CO., ROCHESTER, N. Y., U.S.A.

NEW from SWIFT!

Bannister

So tempting they awaken any baby's natural liking for all meats!

100% Strained Pork with Apple Sauce Added
100% Strained Ham with Raisin Sauce Added
100% Strained Lamb with Mint Flavor Added

Occasionally you hear mothers say, "But my baby just doesn't seem to like meat." Yet you know, and most mothers recognize, that meat brings essential nutritional values to baby's diet.

To help babies like meat, Swift's scientists have created three new varieties of fruit-flavored meats. Each is 100% meat, mildly flavored with just a bit of fruit or mint to make it especially tempting to babies. They're strained wonderfully smooth. They're also high in meat's complete proteins and easy to digest.

And they're as delicious, as nourishing, as Swift's 102 years' experience in fine meats can make them. You can recommend all three with complete confidence. (Available in chopped form for Juniors, too.)

Swift
102nd YEAR
to serve your family better

11 other tasty varieties

Beef · Pork
Ham · Lamb
Liver & Bacon
Chicken · Veal
Liver · Heart
Egg Yolks
Egg Yolks & Bacon

Meats for Babies Swift's most precious product

New

liquid pediatric analgesic-antipyretic

Liquiprin*

for children

safer than aspirin, easier to use

for infants' and children's fever, discomfort of colds, minor aches and pains and following immunizations.

LIQUIPRIN is a suspension of salicylamide—chemically and pharmacologically distinctive from aspirin and other salicylates. Clinically, its analgesic-antipyretic action is approximately the same as that of aspirin, but its therapeutic action does not depend on conversion to salicylate, salicylic acid or their metabolites.

LIQUIPRIN offers these major advantages:

1. safer than aspirin
2. less gastric irritation
3. helps calm the feverish, fretful child
4. easier on the child with gastrointestinal upset
5. more rapidly absorbed
6. relieves minor aches and pains—reduces fever

administration: Convenient liquid form, pleasant taste and calibrated dropper make for easy accurate administration...directly from dropper or mixed with fruit juice, formula or milk. Each ½ dropper contains 1¼ gr. of salicylamide.

dosage: ½ dropper for each year of age, not to exceed 2 droppers (5 gr.).

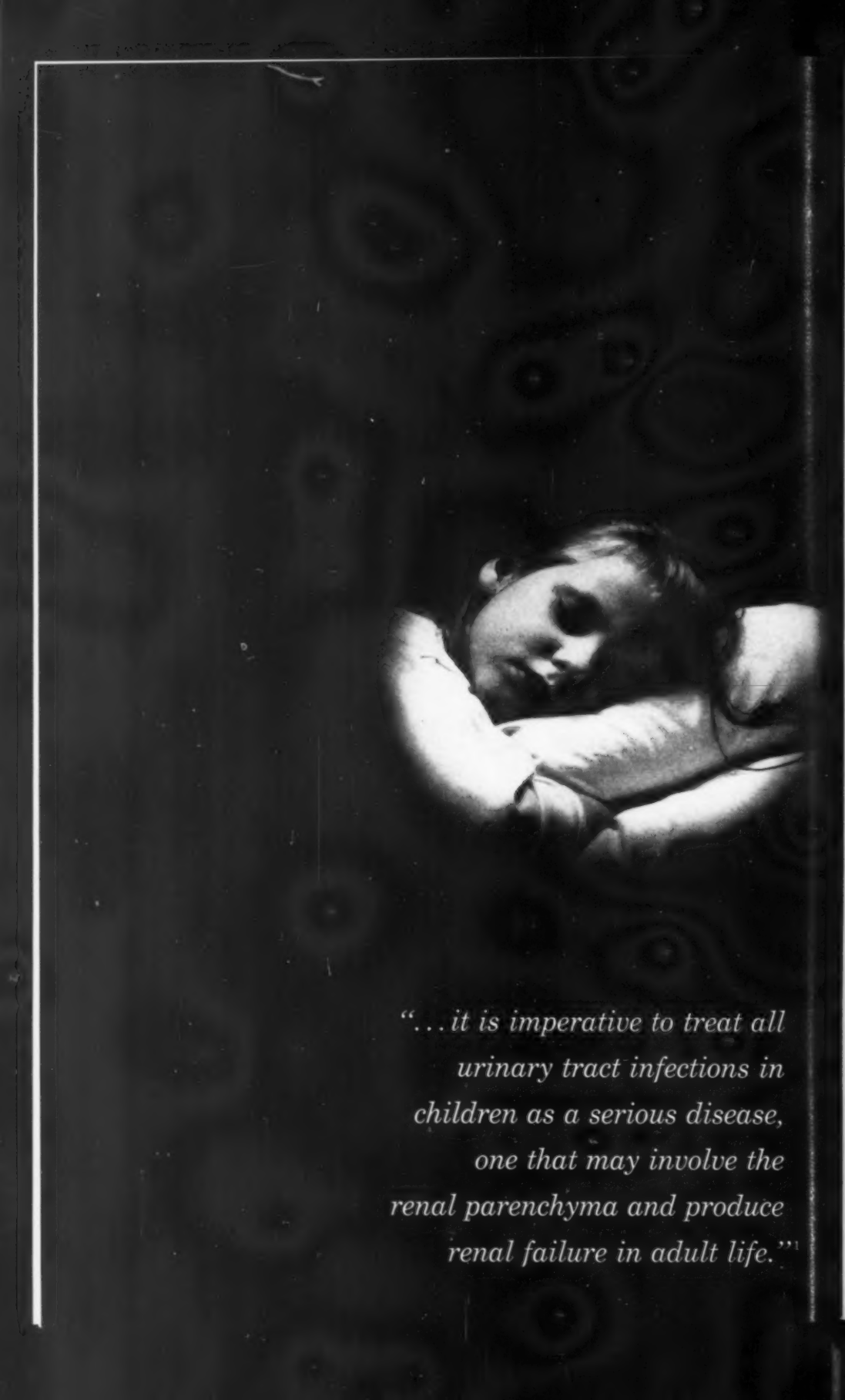
added safety: LIQUIPRIN is supplied in non-spill safety bottles. LIQUIPRIN is safer than aspirin—and made safer still because children cannot pour or drink the medication from this new, **exclusive** safety container.

available: bottles of 50 cc., 1 gr. salicylamide per cc.

bettering baby care through specialized research

*TRADEMARK FOR SALICYLAMIDE SUSPENSION. JOHNSON & JOHNSON.

Johnson & Johnson



"...it is imperative to treat all urinary tract infections in children as a serious disease, one that may involve the renal parenchyma and produce renal failure in adult life."[1]

"an effective urinary antibacterial agent in children."[2]

FURADANTIN®

brand of nitrofurantoin

In children, since "chronic urinary infection is generally the sequel of inadequately treated acute infection,"[3] prompt and adequate therapy with FURADANTIN can prevent irreparable renal damage. FURADANTIN also "has been a safe and effective therapeutic and prophylactic drug for chronic urinary tract infection. . . . We feel the drug should be continued prophylactically for a minimum of several months after the urine has been sterilized."[1]

FURADANTIN has "yielded a number of striking results in clearing up resistant infections [in children] particularly with A. aerogenes, Pseudomonas aeruginosa, and a few cases of B. proteus. It is generally well tolerated in the recommended dosage schedule."[4]

In the treatment of Proteus infections, "FURADANTIN Pediatric Suspension [Oral Suspension] 1 teaspoonful four times daily, is the most satisfactory medication, if tolerated. . . . It can be given over a long period without ill effects and is excreted in large amounts in the urine."[5] In one study, FURADANTIN proved much more effective than any other drug used previously in the treatment of Proteus infections. "We feel that this is especially important since P. vulgaris infections occur rather commonly in infants and children."[2]

In addition to unexcelled effectiveness against a wide range of gram-positive and gram-negative bacteria, FURADANTIN has a wide margin of safety. Well tolerated, FURADANTIN has proven nontoxic to kidneys, liver and blood-forming organs. No cases of monilial superinfection, crystalluria, or staphylococcic enteritis have ever been reported. In 6 years of extensive use, development of bacterial resistance remains negligible.

AVERAGE FURADANTIN DOSAGE

FURADANTIN ORAL SUSPENSION (25 mg. per 5 cc. tsp.) : Average daily dose for children between 15 and 75 lbs., using 5 cc. teaspoon, is given below. Administered 4 times daily with food or milk, it is readily miscible with water, infants' formulae, milk or fruit juices.

15-24 lbs. (7-10 Kg.)	*25-49 lbs. (11-22 Kg.)*	*50-74 lbs. (23-33 Kg.)*	*75 lbs. (34 Kg.)*
½ teaspoonful q.i.d.	*1 teaspoonful q.i.d.*	*2 teaspoonfuls q.i.d.*	*3 teaspoonfuls q.i.d.*

Supplied: Bottle of 60 cc.

FURADANTIN TABLETS: Average dose for children is 5 to 7 mg. per Kg. (2.3 to 3.2 mg. per lb.) in 4 divided doses daily.

Supplied: Tablets of 50 mg. and 100 mg., bottles of 25 and 100.

NOW for hospitalized patients, for severe urinary tract infections when peroral administration of FURADANTIN is not feasible and for serious infections as septicemia (bacteremia) when the bacterium is sensitive.

NEW, LIFESAVING **FURADANTIN** *Intravenous Solution*

REFERENCES: 1. Marshall, M., Jr., and Johnson, S. H., III.: J. Urol., Balt. 76:123, 1956. 2. Johnson, S. H., III, and Marshall, M. Jr.: A. M. A. Am. J. Dis. Child. 89:199, 1955. 3. Campbell, M. F.: Modern Med. 24:85, 1956. 4. Engel, W. J.: Med. Clin. N. America, p. 965 (July) 1955. 5. Carroll, G.: Pediat. Clin. N. America, p. 781 (Aug.) 1955.

FURADANTIN SENSI-DISCS

for bacterial sensitivity tests are available from Baltimore Biological Laboratories.

NITROFURANS . . . a *new* class of antimicrobials . . .
neither antibiotics nor sulfonamides

EATON LABORATORIES, NORWICH, N. Y.

for those cold-weather infections

Compocillin-V®

. . . gives patients the higher blood levels of penicillin V in two appealing forms . . . easy-to-swallow Filmtabs® and tasty, banana-flavored suspension

Filmtabs (Potassium penicillin V, Abbott) come in 125 mg. (200,000 units), bottles of 50, and in 250 mg. (400,000 units), bottles of 25. Oral Suspension (Hydrabamine penicillin V, Abbott) contains 180 mg. (300,000 units) per 5-cc. teaspoon, in 40-cc. and 80-cc. bottles. Abbott

® FILMTAB—FILM-SEALED TABLETS, ABBOTT; PAT. APPLIED FOR.

This is Article No. 4 in a series of six devoted to foot problems common to children's feet. (4)

Pigeon-Toe In

A common lower extremity problem encountered in childhood is the disorder usually referred to as "pigeon-toe." The child suffering from this condition displays an awkward gait characterized by marked adduction of the feet.

The construction of the ankle and subastragalus joints is such that the foot reaches its maximum degree of adduction when in full extension. Consequently, the deformity is usually exaggerated in running or rapid walking. The child frequently trips himself and falls.

Pigeon-toe may arise from factors present in the foot itself, or may be the result of abnormalities elsewhere in the lower extremity. The causes in the foot include metatarsus varus, evasive factors such as a painful pronation, and tumors or excrescences such as helomata or verrucae. Evasion factors are conditions which cause the child to adduct the foot and place the weight on the foot's outer border for the purpose of avoiding pain. Pigeon-toe may also be secondary to lesions occurring more proximally in the extremity, such as

Continued on opposite page

Child Life
SHOES

CHILD LIFE regular shoes, such as Oxford No. 266, are readily adaptable for corrective wedging because they are all leather, welt constructed shoes of the finest quality and workmanship.

A Reprint Of This Series Is Offered

A reprint of this article — and the other five in this continuing series — is available, without charge or obligation, at your request. The subjects individually covered are *Pronation in Pre-School and Early Childhood, Pronation in Adolescence, Pigeon Toe, Knockknees and Bow Legs, and Painful Heel.*

Yours For The Asking

A wedge chart, prepared for the professional man, illustrating corrective wedges and describing their work is yours for the asking.

A booklet on the care of the feet and advice on the selection of children's shoes will be sent to you in quantity at your request. This booklet — completely non-commercial — is suitable for presentation to young mothers in your practice.

The Child

by A. Rubin, D.S.C.* John T. Sharp, D.S.C.†

torsional structures adjacent to the hip, such as the tensor fascia lata, or inequality in extremity length. In the last instance, the pigeon-toe is usually present on the short side.

Treatment of pigeon-toe will depend upon the cause. Consequently, the first step in its management is careful examination for the purpose of determining the etiology of the disorder.

Metatarsus varus is a deformity which is apparently on increase in recent years. It has been suggested that the present emphasis on vitamin therapy for the pregnant mother may contribute to this increase, in that such therapy is thought to prevent the foot from going into the more serious full-blown talipes equinovarus deformity, which is on the decrease. Dr. J. H. Kite has suggested that metatarsus varus is actually a part of the talipes equinovarus deformity. Two forms are usually recognized: a severe form with marked forefoot adduction and inversion and fixed valgus of the heel, and a milder form, less rigid, with a lesser degree of forefoot adduction and no fixed heel valgus. The severe type tends to be hereditary, is extremely intractable, and is strongly inclined to recur; the milder type is not hereditary, is fairly easy to correct, and generally does not recur.

The severe forms of metatarsus varus generally respond only to surgical procedures. The milder variety usually is successfully treated by such measures as wedge casting, use of the Dennis-Browne type splint, exercise, and shoe therapy. A common type of shoe used is the reverse last shoe which forces the forefoot into an abducted position.

Pigeon-toe secondary to torsional deformities in the extremity will usually respond to the Dennis-Browne splint in conjunction with proper shoe-wedging. (See illustration.)

Wedges may vary in thickness from 1/8" to 1/4" depending upon the age of the child and severity of the deformity.

In instances where the pigeon-toe is the result of an evasion mechanism, such as painful pronation, elimination of the exciting cause will often result in its correction. Occasionally in the very young child, pigeon-toe will represent a temporary retention of the intrauterine position of the extremity. In uncomplicated cases correction of these forms is often spontaneous.

It is well to remember that in all instances where the pigeon-toe present is associated with internal torsional deformities of the extremity, there must be constant control of sleeping and sitting postures of the child. Attitudes which tend to encourage internal rotation, such as belly-sleeping with the feet adducted, or sitting on the inverted foot, must be prevented if satisfactory results are to be obtained.

Common shoe wedgings are illustrated. Most other wedgings also prove effective, since the limb is toward one extreme of attitude, and postural alterations would of necessity tend towards normalcy. Frequent examinations in the early stages of treatment should be made since individual responses vary.

REFERENCES

(1) Kite, J. H.: Theories on the Increase in the Occurrence of Congenital Metatarsus Varus Deformity. Amer. Acad. Orthoped. Surgeons: Instructional Course Lectures, v. VII, 1950.

(2) Kite, J. H.: Congenital Metatarsus Varus — A Study Based on Four Hundred Cases. Amer. Acad. Orthoped. Surgeons: Instructional Course Lectures, v. VII, 1950.

*Secretary, National Association of Chiropodists, and Editor of its Journal. Formerly Director of the Foot Clinics, and Professor and Chief of Orthopedic Dept., Illinois College of Chiropody and Foot Surgery.

†Professor of Chiropodal Pediatrics, Temple University, School of Chiropody.

* ■ WEDGED AREA ——— LONG COUNTER

------- THOMAS HEEL

(4) Published in the interest of pediatricians as refresher reading by

HERBST Shoe Manufacturing Co., Milwaukee 45, Wisconsin

For Speedier Return To Normal Nutrition

Meat...

and the Protein Need in Renal Disease

Prevailing opinion holds that during the nephrotic state—provided the kidneys are capable of excreting nitrogen in a normal manner—the patient should be given a diet high in protein (1.5 to 2 grams per kilogram of body weight daily). The purpose of such a diet is to replace depleted plasma protein and to increase the colloidal osmotic pressure of the blood.

Sharp restriction of dietary salt appears indicated only in the presence of edema, but moderate restriction is usually recommended.

Lean meat is admirably suited for the diets prescribed in most forms of renal disease. It supplies relatively large amounts of high quality protein and only small amounts of sodium and chloride. Each 100 Gm. of unsalted cooked lean meat (except brined or smoked types) provides approximately 30 Gm. of protein, and only about 100 mg. of sodium and 75 mg. of chloride.

In addition to its nutritional contributions meat fulfills another advantageous purpose: It helps make meals attractive and tasty for the patient who must rigidly adhere to a restricted dietary regimen.

The nutritional statements made in this advertisement have been reviewed by the Council on Foods and Nutrition of the American Medical Association and found consistent with current authoritative medical opinion.

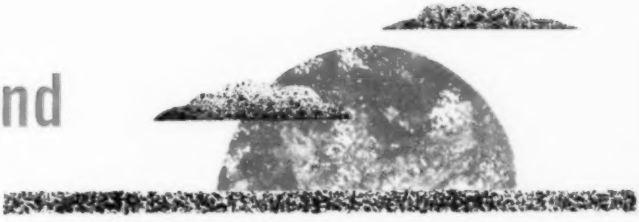
American Meat Institute
Main Office, Chicago . . . Members Throughout the United States

just

two doses

A. M.

and



P. M.

LIPO GANTRISIN

ROCHE

...and you can be sure that your patients will have prompt, lasting plasma and urine levels.

the regimen is simple
when you prescribe

LIPO GANTRISIN

Lipo Gantrisin is the ideal pediatric form of Gantrisin, in which 2 doses a day are sufficient to combat most urinary and systemic infections of non-viral—non-rickettsial origin. Follow this regimen and note the quick response.

Dosage: Teaspoonfuls every 12 hours

Children 20 lbs — 1 60 lbs — 2
40 lbs — 1½ 80 lbs — 3

Adults . . . 4 or 5 (no alkalies or fluids need be given)

Lipo Gantrisin® Acetyl — brand of acetyl sulfisoxazole in a homogenized mixture

ROCHE LABORATORIES • DIVISION OF HOFFMANN-LA ROCHE INC • NUTLEY 10 • N.J.

ROCHE—REG. U. S. PAT. OFF.

selected platelets make a select powder

PROOF

2

Only Johnson's Baby Powder uses purest Italian talc exclusively. The unique flat crystalline talc platelets are then skillfully processed for uniformity.

Uniform flat platelets lubricate skin smoothly, don't roll, scatter and fall to cause irritating chafing.

Forms a tight cloud effect with special additional process that discards particles likely to be irritating.

bettering baby care through specialized research

BABY PRODUCTS DIVISION

Johnson & Johnson

Johnson's

BABY POWDER

. . . it was wonderful seeing you all. Do you realize, it was the first time since the baby came that I had an evening out? I enjoyed every minute of it . . .

an evening out . . . with

SIMILAC®

as the "relief" bottle

A morale builder

Whether it is a frequent or an occasional feeding, Similac makes an excellent "relief" bottle for the breast-fed infant. Because a new baby, particularly a first baby, changes the family's habit patterns, it is important that the mother not always feel "chained down." An occasional evening out is a necessary and valuable respite for her health and morale. Otherwise, the mother's tensions may increase.

Assurance for the breast-feeding mother

When she is reassured that Similac is closely equivalent to her own milk, and that breast feedings can be compatibly replaced with Similac feedings, the mother will feel secure in using Similac for a relief bottle.

A compatible supplement

Similac provides physiologic levels of essential fatty acids, protein and carbohydrate in the same balanced proportions as in breast milk. All known essential vitamins also are included.

This advertisement conforms to the Code for Advertising of the Physicians' Council for Information on Child Health.

Compatible infant feeding—breast feeding and Similac®

ROSS LABORATORIES
Columbus 16, Ohio

RESEARCH SERVICE Ross NUTRITION

MEAD JOHNSON

SYMBOL OF SERVICE IN MEDICINE

you can select his level of vitamin protection from

the Vi-Sol Vitamin Family

Dropper dosage

Tri-Vi-Sol® 3 basic vitamins

Poly-Vi-Sol® 6 essential vitamins

Deca-Vi-Sol® 10 significant vitamins with stable B_{12} in solution with C.

Pleasant fruit-like flavors • hypoallergenic

stable • require no refrigeration

unbreakable plastic 'safti-dropper'

VS47B

Whenever tetracycline therapy is indicated—

Every clinical consideration recommends

Tetrex®

THE ORIGINAL TETRACYCLINE PHOSPHATE COMPLEX

U.S. PAT. NO. 2,701,900

for faster, more certain control of infection

- A single, pure drug (not a mixture)
- High tetracycline blood levels
- Clinically "sodium-free"
- Equally effective, b.i.d. or q.i.d.
- Exceptionally free from adverse reactions
- Dosage forms for every therapeutic need

BRISTOL LABORATORIES INC., SYRACUSE, NEW YORK

Available for your prescription at all leading pharmacies

baby's best bodyguard

AMMENS® gives soothing protection to babies' tender skin. And when diaper rash, prickly heat or other skin irritations make him restless, AMMENS eases discomfort, promotes healing.

AMMENS contains starch, widely and uniformly dispersed in talc for maximum absorption of moisture; oxyquinolin and zinc oxide protect macerated crevices against bacterial invasion.

AMMENS is fluffy, white, and smells good, too. Tell baby's mother to keep a can of AMMENS handy.

AMMENS® *MEDICATED* POWDER

Bristol-Myers Company, 19 West 50 Street, New York 20, N. Y.
Distributor for Charles Ammen Co., Alexandria, La.

In urinary-tract infections

HIGH TISSUE LEVELS

HIGH BLOOD LEVELS

LOW TOXICITY

Wyeth®
Philadelphia 1, Pa.

SUSPENSION TABLETS

SULFOSE®

Trisulfapyrimidines, Wyeth
(Sulfadiazine, Sulfamerazine, Sulfamethazine)

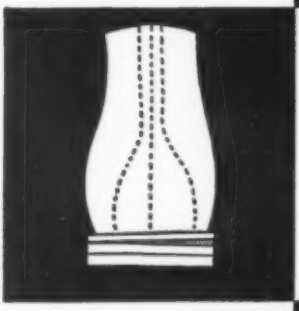
Quality at your feet...

BROWN
SHOE COMPANY

Propr-Bilt has the built-in fit features you want in children's shoes

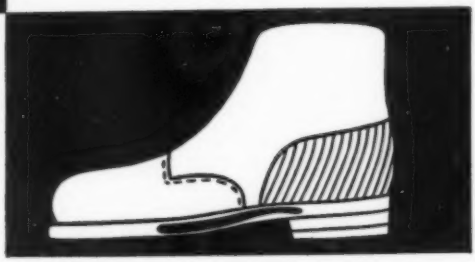
You can recommend them with confidence

Sole is straight along medial or inner aspect. Round toe for spread and free function of toes. Width at ball of foot allows for generally short and plump shape of children's feet.



Heel seat and counter are narrow for snug fit. In sizes up to 8 (except in long-counter Thomas-heel shoes) heel is wedged to give more support to the long arch.

Propr-Bilt steel shank (used only in sizes above 8) is shaped to the last, so arch is adequately supported on medial side. Uppers in infant's sizes reach above the ankle and are always of blucher design.



A complete line of feature shoes
backed by the Buster Brown reputation for quality.

PROPR-BILT

by the makers of
BUSTER BROWN.

they know what they like

you know what they need for comprehensive vitamin protection

Deca-Mulcin®

delicious orange-flavored teaspoon dosage of 10 nutritionally significant vitamins

- assured stability, including B_{12}
- non-sticky, free flowing
- no refrigeration required
- pouring lip bottles of 4, 8 and 16 oz.

Deca-Vi-Caps®

small easy-to-swallow capsules of 10 nutritionally significant vitamins

- potency assured
- inviting red color
- store anywhere
- bottles of 30 and 100

and for the dropper-dosage age – Specify Deca-Vi-Sol®

These three Deca Family Products have the same basic formulation and the same standard of comprehensive protection. The basic family name Deca is easy to remember and simplifies specification during the vital first decade.

MEAD JOHNSON
SYMBOL OF SERVICE IN MEDICINE

35787

to quiet
the cough
and calm
the patient...

Comprehensive action, comprehensive relief

Expectorant action
Antihistaminic action
Sedative action
Topical anesthetic action

PHENERGAN®

EXPECTORANT

Promethazine Expectorant
With Codeine Plain (without Codeine)

Wyeth®
Philadelphia 1, Pa.

PHYSICIANS' COUNCIL FOR INFORMATION ON CHILD HEALTH

This advertisement conforms to the Code for Advertising of the Physicians' Council for Information on Child Health.

Wherever high protein-low fat diets are indicated, prescribe Hi-Pro. For the premature, in diarrheas or for fat intolerance feeding difficulties, Hi-Pro's balanced formula assures high protein with low fat and moderate carbohydrate intake.

Hi-Pro is a low cost, spray dried, specially processed, partially delactosed whole and defatted cow's milk . . . readily digested and assimilated. For rapid growth and firm tissue turgor, prescribe Hi-Pro. Write for samples and further information.

Serving the medical profession since 1934.

JACKSON-MITCHELL *Pharmaceuticals, Inc.*
10401 Virginia Avenue, Culver City, California

HI-PRO
approximate analysis
Protein . . . 41.0%
Fat 14.0%
Lactose . . . 36.0%
Available in 1 and 25 lb. vacuum-packed tins

Sarah Bernhardt as Hamlet

IN SUBACUTE AND CHRONIC DERMATOSES
(Regardless of Previous Refractoriness)

TARCORTIN®

Hydrocortisone in Coal Tar Extract (TARBONIS®) Cream

Topical hydrocortisone alone or other newer steroids alone often produce dramatic but temporary results.[1-3] TARCORTIN, however, adds greater permanence to initial success.[2-3] The broader and more enduring results with TARCORTIN derive from the potentiating effect of its components—tar and hydrocortisone.

PACKAGE: 7 gram and 1 ounce tubes.

FORMULA: 0.5% Hydrocortisone in 5.0% Special Coal Tar Extract (TARBONIS) in a Greaseless, Stainless, Hydrophilic, Vanishing Cream.

BIBLIOGRAPHY:
(1) Welsh, A. L., and Ede, M.: Hydrocortisone Ointments: Their Rational Use in Dermatology, Ohio State M. J. 50:837 (Sept.) 1954. (2) Clyman, S. G.: The Comparative Effects of Hydrocortisone and Hydrocortisone-Coal Tar Extract (Tarcortin) Creams in Atopic Dermatitis. Postgrad. Med. (Mar.) 1957. (3) Abrams, B. P., and Shaw, C.: Atopic Dermatitis Treated with Tar-Steroid (Tarcortin) Cream—A Case Report, Clin. Med. 3:839 (Sept.) 1956.

INDICATED WHERE INFECTION IS PRESENT OR ANTICIPATED AND FOR DRY, SCALY ECZEMAS

New NEO-TARCORTIN® OINTMENT

HYDROCORTISONE, NEOMYCIN AND SPECIAL COAL TAR EXTRACT (TARBONIS)

PACKAGE: 7 gram and 1 ounce tubes.

FORMULA: 0.5% Hydrocortisone, 0.35% Neomycin (as Sulfate) and 5.0% Special Coal Tar Extract (TARBONIS).

REED & CARNRICK Jersey City 6, New Jersey

W

Meyenberg
GOAT MILK

specific vitamin
therapy from
the express wagon
set to the juke box
Jills and Joes

SQUIBB introduces

THERAGRAN junior

SQUIBB VITAMINS FOR THERAPY

now . . . the time-tested, clinically proved Theragran formula especially adapted and encapsulated to meet your needs for vitamin therapy in children and adolescents

Each small, easy-to-take Theragran Junior capsule supplies:

Vitamin A	5000 U.S.P. units
Vitamin D	1000 U.S.P. units
Thiamine mononitrate	5 mg.
Riboflavin	5 mg.
Niacinamide	30 mg.
Ascorbic acid	100 mg.
Pyridoxine hydrochloride	2 mg.
d-Calcium pantothenate	3 mg.
Vitamin B_{12} activity concentrate	10 mcg.

DOSAGE:

1 or 2 capsules daily, or as directed by the physician.

SUPPLY:

Bottles of 30 and 100 capsules.

Other members of the distinguished Theragran family:

THERAGRAN
THERAGRAN-M
THERAGRAN LIQUID

SQUIBB *Squibb Quality—the Priceless Ingredient*

"THERAGRAN" IS A SQUIBB TRADEMARK

paired for wider range of antibacterial action

ILOTYCIN-SULFA

(Erythromycin with Triple Sulfas, Lilly)

PEDIATRIC

in palatable oral suspension

Effective against a wide range of gram-positive and gram-negative pathogens. The combination of 'Ilotycin' (Erythromycin, Lilly) and the triple sulfonamides is particularly useful in the management of mixed respiratory and genito-urinary tract infections. 'Ilotycin-Sulfa' is notably safe and well tolerated.

***Supplied** as a tasty oral suspension providing in a 5-cc. teaspoonful 200 mg. of 'Ilotycin' as the ethyl carbonate plus 167 mg. each of sulfadiazine, sulfamerazine, and sulfamethazine.*

ELI LILLY AND COMPANY • INDIANAPOLIS 6, INDIANA, U.S.A.

732196

KIDS LOVE 'EM*

*WORMS HATE 'EM

No fasting • No special diets • No purging

The new Piperazate Wafers, utilizing less toxic, insoluble piperazine *phosphate*, provide the shortest, most pleasant piperazine treatment yet developed for intestinal helminths. For pinworm, *only one dose a day* for just *one week* is required; for roundworm, a *single dose*.

Kids love the cool, tasty mint flavor of Piperazate Wafers. There is no possibility of spillage or variation in the size of the dose. And the use of Piperazate avoids the high incidence—35-50%—of nausea, vomiting and diarrhea associated with gentian violet therapy.[1]

Piperazate assures a 90% cure rate in one week's treatment of pinworm[2] and an 85% cure rate in one day's treatment of roundworm.[3]

One Week Dosage for Pinworm		**One Day Dosage for Roundworm**	
Children 15-30 lbs.	1 Wafer	Children 20-30 lbs.	3 Wafers
Children 31-60 lbs.	2 Wafers	Children 31-40 lbs.	4 Wafers
Children 61 lbs. and over	4 Wafers	Children over 40 lbs. and adults	7 Wafers
To be sucked or chewed before breakfast for 7 consecutive days.		To be taken at one time on one day only.	

New

Piperazate* Wafers

piperazine phosphate, Leeming, 500 mg.

Supplied:
In packages
of 28 Wafers

1. Goodman, L., and Gilman, A.: Pharmacological Basis of Therapeutics, New York, Macmillan, 1955, p. 1153. 2. Brown, H. W., et al: J. A. M. A. *161:* 515 (June) 1956. 3. Hoekenga, M. T.: World Med. J. *3:* (Sept.) 1956.

*TRADEMARK

Thos. Leeming & Co. Inc. 155 East 44th Street, New York 17, N. Y.

INFANTILE ECZEMA

...soothed by AVEENO* Colloid Baths

. . . convert the baby's bath into a demulcent and sooth medium by adding a tablespoon or two of AVEENO Colloidal Oatmeal . . . the oatmeal concentrate developed especially to soothe and calm delicate skin.

...cleansed by AVEENO* Colloid Baths

. . . The unique dirt-adsorbing action of Aveeno Colloi Oatmeal picks up and removes skin dirt without penetration of the protective layers of the skin. AVEENO Colloid Baths, therefore, eliminate the need for irritating soaps.

*AVEENO Colloidal Oatmeal is available in 18 oz. and 4 lb. boxes

For samples mail this card

Please send me samples of

☐ **Aveeno Colloidal Oatmeal**
. . . for soothing Colloid Baths

☐ **Aveeno Ointment**
. . . Lassar's Paste—MODERNIZED

Name_____

Address_____

City and State_____

7

because it contains *soothing* Aveeno Colloidal Oatmeal

AVEENO OINTMENT

SUPERIOR to Lassar's Paste

... in calming irritated skin

... in absorbing exudates

... in ease of application

ACTIVE INGREDIENTS
Aveeno Colloidal Oatmeal, zinc oxide and 0.5% hexachlorophene (to protect against bacterial invasion)... in an emollient base.

Aveeno Ointment is available in 1 oz. tubes

Postage Will be Paid by Addressee

No Postage Stamp Necessary If Mailed in the United States

BUSINESS REPLY CARD
First Class Permit No. 47133 Sec. 34.9, P. L. & R., N. Y., N. Y.

AVEENO CORPORATION
250 WEST 57th STREET
NEW YORK 19, N. Y.

Send this card for samples of

Aveeno Colloidal Oatmeal
... for soothing Colloid Baths

Aveeno Ointment
... Lassar's Paste—MODERNIZED

COMFORT IN COLD, GRIPPE, "FLU"

time for **Tyzine®**

brand of tetrahydrozoline hydrochloride

For superior relief of NASAL CONGESTION

Proved in more than 2400 published cases... virtually immediate effect lasting as long as six hours... no rebound congestion... odorless, tasteless, no sting, burn or irritation.

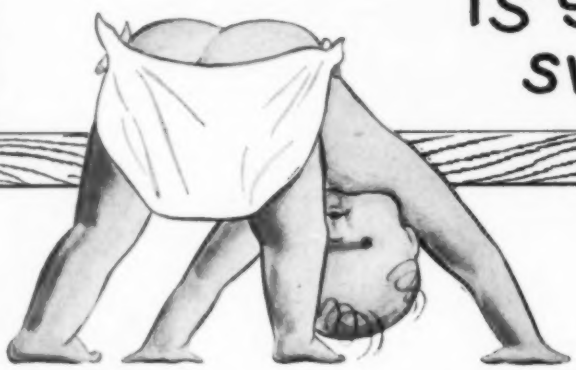
Tyzine® Nasal Solution, 1-oz. dropper bottles, 0.1%. Nasal Spray, 15 cc., in plastic bottles, 0.1%. Pediatric Nasal Drops, 1/2-oz. bottles, 0.05%, with calibrated dropper.

Note: As with certain other widely used nasal decongestants, overdosage may cause drowsiness or deep sleep in infants and young children: KEEP OUT OF HANDS OF CHILDREN OF ALL AGES. Tyzine Nasal Spray and Tyzine Nasal Solution, 0.1%, are not recommended for use in children under six. When using Tyzine Nasal Spray in the plastic bottle, it should be administered only in an upright position.

Pfizer PFIZER LABORATORIES, Brooklyn 6, New York
Division, Chas. Pfizer & Co., Inc.

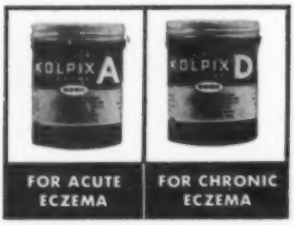
LOOK MA!

NO MORE DIAPER RASH that **ACID MANTLE®** IS SURE SWELL!



Baby's sensitive skin is best protected by the use of **ACID MANTLE – CREME or LOTION – pH 4.2.** It instantly restores normal acidity to the skin which has been made alkaline, due to contact with urine. It thus prevents diaper rash.

AVAILABLE: Creme in 4 oz. plastic jar, Lotion in 4 oz. plastic squeeze bottle.



KOLPIX® A AND D CREMES

Whole crude coal tar in the exclusive Acid Mantle base. "Medium gray color instead of black and the base is not greasy but water soluble. Kolpix A is for acute, somewhat active eczema, Kolpix D for chronic eruptions. These are fine preparations – I use them a great deal."* 1 oz. tubes, 2 and 4 oz. jars.

INCORPORATED IN EXCLUSIVE ACID MANTLE® VEHICLE

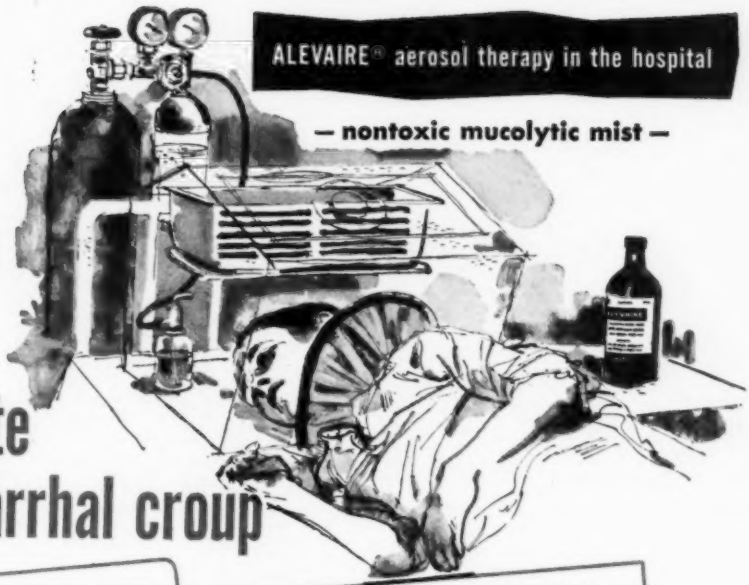
*Lewis Webb Hill, M.D., "Treatment of Eczema in Infants and Children," Journal of Pediatrics, vol. 47, no. 6, Dec. 1955

DOME *Chemicals Inc.*

109 WEST 64 ST., NEW YORK 23, N.Y. In Canada: 2765 Bates Rd., Montreal, P.Q.

ALEVAIRE® aerosol therapy in the hospital

— nontoxic mucolytic mist —



acute catarrhal croup

CASE REPORT*

D D., a 2 year old male with fever, cough and laryngeal stridor of one day's duration, was hospitalized because of continued respiratory distress. Treatment had consisted of penicillin, injections and wet vapor inhalations.

Auscultation on arrival revealed harsh breath sounds on both sides and coarse rhonchi. Continuous crouping cough caused severe respiratory distress; the pharynx was injected and the tonsils were large. Diagnosis was acute catarrhal croup.

The child was placed in a croup tent with a humidifier, and antibiotics were administered. The condition did not change and Alevaire aerosol was begun in the evening. The cough gradually became easier and less frequent. The next day he rested comfortably, his temperature was reduced, no respiratory distress was noted, and the lungs were almost clear on auscultation. A day later no further therapy was required and the child was discharged on the fourth day after admission.

*Smessaert, Andre; Collins, V.J.; and Kracum, V.D.: *New York Jour. Med.*, 55:1587, June 1, 1955.

ALEVAIRE

Alevaire is supplied in bottles of 60 cc. for intermittent therapy and in bottles of 500 cc. for continuous inhalation therapy.

Winthrop LABORATORIES
NEW YORK 18, N. Y. • WINDSOR, ONT.

Alevaire, trademark reg. U.S. Pat. Off.

has been dramatically effective in:

- neonatal asphyxia (due to inhalation of amniotic fluid, mucus obstruction, atelectasis)
- croup • laryngitis • tracheobronchitis
- pertussis • pneumonia • bronchial asthma
- emphysema • bronchiectasis • lung abscess
- pneumoconiosis • smoke, kerosene poisoning
- poliomyelitis (respiratory complications)
- routine oxygen therapy • tracheotomy
- prevention of postoperative pulmonary complications

Most patients under stress will welcome Ovaltine as part of their diet

Ovaltine provides a wealth of essential nutrients which help the body resist the detriment of stressful states. Ovaltine's natural blandness combined with good taste makes it especially valuable in many bland diets.

Ovaltine is a soothing, nourishing, well-tolerated beverage that's ideal for use in many stress states where stimulating beverages are usually contraindicated.

Patients like Ovaltine hot or cold, at any time of the day.

Three servings of Ovaltine and milk provide:

MINERALS		VITAMINS	
*Calcium	1.12 Gm.	*Vitamin A	4000 I.U.
Phosphorus	940 mg.	*Vitamin D	420 I.U.
*Iron	12 mg.	*Ascorbic acid	37.0 mg.
Copper	0.7 mg.	*Thiamine	1.2 mg.
Iodine	0.2 mg.	*Riboflavin	2.0 mg.
Fluorine	0.5 mg.	Pyridoxine	0.5 mg.
Cobalt	0.006 mg.	Vitamin B_{12}	5.0 mcg.
Sodium	560 mg.	Pantothenic acid	3.0 mg.
Chlorine	900 mg.	*Niacin	10.0 mg.
Magnesium	120 mg.	Folic acid	0.05 mg.
Manganese	0.4 mg.	Choline	200 mg.
Potassium	1300 mg.	Biotin	0.03 mg.
Zinc	2.6 mg.		
		*PROTEIN	32 Gm.
		CARBOHYDRATE	65 Gm.
		FAT	30 Gm.

*Nutrients for which daily dietary allowances are recommended by the National Research Council.

Ovaltine®

The World's Most Popular Fortified Food Beverage

The Wander Company, 105 W. Adams St., Chicago 3, Ill.

when you want Broad-Spectrum Benefits . . .

When you want extended antibacterial coverage with high relative safety, consider PEN·VEE SULFAS. Consider how it permits you to reserve the conventional broad-spectrum antibiotics for the resistant infections specifically requiring them. Consider PEN·VEE SULFAS because it unites penicillin V and sulfapyrimidines for potent complementary action. Prescribe it for wide antimicrobial attack in mixed infections and those not readily diagnosed.

Supplied: PEN·VEE SULFAS Tablets, bottles of 36. Each tablet contains 90 mg. (150,000 units) of penicillin V, 0.25 Gm. of sulfadiazine, and 0.25 Gm. of sulfamerazine. PEN·VEE SULFAS for Suspension, bottles of 2 fl. oz. upon reconstitution. Each 5-cc. teaspoonful after reconstitution contains 90 mg. (150,000 units) of benzathine penicillin V, 0.25 Gm. of sulfadiazine, and 0.25 Gm. of sulfamerazine.

Wyeth®
Philadelphia 1, Pa.

PEN·VEE® SULFAS

Tablets: Penicillin V (Phenoxymethyl Penicillin) and Sulfonamides
For Suspension: Benzathine Penicillin V and Sulfonamides

"Infantile Colic Is A Common Clinical Entity Which Cannot Be Ignored" [1]

Intolerances to added carbohydrate and to butterfat cause a greater incidence of infantile colic than any other factor. In fat intolerance, it is probably the type of fat and not the quantity that is the responsible factor.[1]

VARAMEL eliminates these troublesome factors because

- ✓ The butterfat is completely replaced by more readily tolerated vegetable fats.
- ✓ No carbohydrate has been added, enabling the physician to select the most suitable sugar for each individual infant, or to prescribe a formula without added sugar.
- ✓ Adequate vitamin fortification eliminates possible digestive disturbances from supplemental vitamin preparations.

In addition, **VARAMEL** is made *exclusively* from Grade A milk and is the only product which offers the physician *complete* flexibility in the control of carbohydrate *plus* the complete elimination of troublesome butterfat.

Approximate Analysis 32 Calories per fl. oz.

Protein	4.9%	Calcium	0.19	Moisture	79.8
Carbohydrate	8.3	Phosphorus	0.15	Ash	1.2
Fat	5.8	Iron	0.0016		

1. Breslow, Lawrence. "A Clinical Approach to Infantile Colic." J. Pediatrics **50** 196 (1957). A copy will be sent on your request.

THE BAKER LABORATORIES, INC.

Milk Products Exclusively for the Medical Profession

Main Office: CLEVELAND 3, OHIO Plant: TROY, WISCONSIN

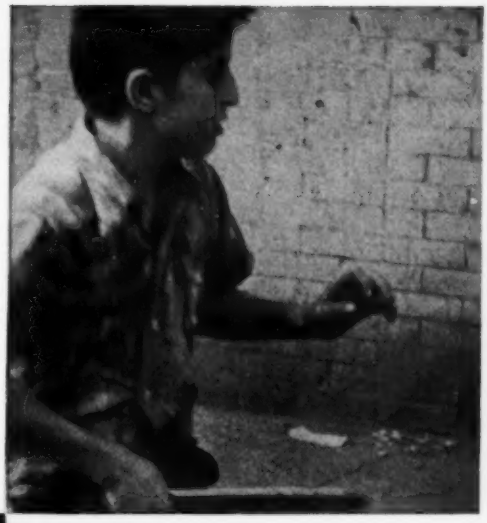
"...disciplinary problem..."

"...temper tantrums..."

"...asthma..."

"...nervousness, stuttering..."

"These are only several of the cases showing a striking response to [ATARAX®]."[1]



ATARAX "lessens tension, relieves symptoms of disturbed autonomic function, and calms hyperkinetic behavior."[2]

Particularly suitable in school children, ATARAX does not cause drowsiness or lassitude...does not impair intellectual function. Almost totally free of side effects.[1-4]

Children like the good taste of ATARAX Syrup. Try ATARAX in your next five cases of childhood emotional problems. Both you and the parents will be pleased with the results.

Dosage: Children, (3 to 6 years), usually one 10 mg. tablet, or one teaspoon syrup, three times daily; (over 6 years), usually two 10 mg. tablets, or 2 teaspoons syrup, 3 times daily. Adults, usually one 25 mg. tablet, or one tablespoon syrup, four times daily.

Supplied: Tablets, tiny 10 mg. (orange) and 25 mg. (green), bottles of 100. Syrup, 10 mg. per tsp., pint bottles. Prescription only.

Bibliography:

1. Nathan, L. A., and Andelman, M. B.: Illinois M. J.: in press. 2. Ayd, F. J., Jr.: read at Symposium on Emotional Problems of Children, Los Angeles, Calif., April 10, 1957. 3. Bayart, J.: presented at International Congress of Pediatrics, Copenhagen, Denmark, July 22-27, 1956. 4. Ayd, F. J., Jr.: New York State J. Med. 57:1742 (May 15) 1957.

in children, too...

PEACE OF MIND ATARAX®

(BRAND OF HYDROXYZINE)

Tablets-Syrup

Roerig New York 17, New York

Put SPARKLE in the EYE

STRENGTH IN THE BONE

for the little sweet-tooth

WHITE'S COD LIVER OIL CONCENTRATE TABLETS

These chewable candy-like tablets make taking cod liver oil a pleasure. Youngsters enjoy the good taste and parents appreciate the low price. Containing 400 units of vitamin D and 4000 units of vitamin A, each tablet equals the vitamin A and D potency of one teaspoonful (5 cc.) of U. S. P. Cod Liver Oil.

Dosage: 2 to 6 tablets daily.
Supplied: Packages of 45; bottles of 100, 240, and 1,000.

for the teething -ring set

WHITE'S COD LIVER OIL CONCENTRATE DROPS

Convenient vitamin A and D therapy for less than a penny daily. Each drop, containing 312 units of vitamin D and 1,560 units of vitamin A, equals the vitamin D potency of 4 cc. of U. S. P. Cod Liver Oil.

Dosage: 2 to 4 drops, placed directly on tongue.
Supplied: Bottles of 8, 30, and 50 cc. with special dropper.

whenever high potency vitamins A and D are indicated

WHITE'S COD LIVER OIL CONCENTRATE CAPSULES

Containing 12,500 units of vitamin A and 1,250 units of vitamin D, each small, easy-to-take capsule equals the vitamin A and D potency of 16 cc. of U. S. P. Cod Liver Oil.

Dosage: As indicated by individual need.
Supplied: Bottles of 40, 100, and 500.

WHITE LABORATORIES, INC. • KENILWORTH, N. J.

In secondary bacterial complications of viral upper respiratory infections

pneumococcal invaders

streptococcal invaders

susceptible staphylococcal invaders

PEN·VEE·*Oral*®

Penicillin V, Crystalline (Phenoxymethyl Penicillin), Wyeth

Wyeth

Philadelphia 1, Pa.

This advertisement conforms to the Code for Advertising of the Physicians' Council for Information on Child Health.

Oral Penicillin with Injection Performance

"...(Dioctyl Sodium Sulfosuccinate) ...has been of great value."[1]

for constipation in children

DOXINATE® SOLUTION 5%

(DIOCTYL SODIUM SULFOSUCCINATE, LLOYD)

THE ORIGINAL DIOCTYL SODIUM SULFOSUCCINATE FOR CONSTIPATION

■ *Treatment*

"...dioctyl sodium sulfosuccinate [Doxinate] has proved useful in the treatment of...constipation in infants and children,..."[2]

"A much more satisfactory medication, which is not a laxative. ..."[1]

■ *Prophylaxis*

"Dioctyl sodium sulfosuccinate...has been employed extensively...in place of mineral oil in order to avoid the formation of dry stools."[3]

The ideal pediatric form... DOXINATE SOLUTION 5%

Doxinate Solution 5% is the only full potency dioctyl sodium sulfosuccinate for fecal softening in children.

Doxinate is gentle, non-irritating and non-habit-forming. It does not inhibit vitamin absorption nor can it produce lipoid pneumonia. The single daily dose of Doxinate Solution 5% is easily administered in milk, formula or fruit juice.

LLOYD *Brothers, Inc., Cincinnati 3, Ohio*

"In the interest of medicine since 1870"

1. Towsley, H. A.: J. Michigan Med. Soc. *54*:1064 (Sept.) 1955.
2. Cass, L. J., and Frederik, W. S.: Am. J. Gastroenterol. (Dec.) 1956.
3. Turell, R.; Pomerantz, A. A., and Denmark, S.M.: Surg. Gynec. & Obstet. *103*:209 (Sept.) 1956.

fever, *discomfort*

under control

with

TYLENOL®

ELIXIR / DROPS

pediatric antipyretic—analgesic

NOW for added ease of administration

TYLENOL ELIXIR—120 mg. (2 gr.) per 5 cc.; bottles of 4 and 12 fl. oz.

TYLENOL DROPS—60 mg. (1 gr.) per 0.6 cc.; 15 cc. bottles with calibrated plastic dropper.

TYLENOL—*the first pediatric dosage form of acetaminophen*

**Reduces fever more quickly and more safely than aspirin*

**Two convenient liquid dosage forms—drops and elixir*

**Well tolerated—children like Tylenol!*

McNEIL LABORATORIES, INC.
Philadelphia 32, Pa.

another pediatric first

NOW...
safer administration

of solutions and
blood with
PLEXITRON®

CONTROLLED VOLUME UNIT

Since 1949, when we introduced the first solutions and equipment specifically for pediatric use, we have continued to anticipate demands for newer pediatric medications and equipment.

The latest development in this field, the 50 cc. **CONTROLLED VOLUME UNIT,** creates a new standard for precision in dosage . . . permits administration in units of 50 cc. . . . safely, surely, accurately . . . without constant supervision.

This flexible-chamber unit fits between bottle and administration set. Only the prescribed contents of the unit can be administered after hemostat is closed. Sterile, nonpyrogenic, expendable, and ready for instant use.

Labor-saving • Time-saving
Trouble-proof in any pediatric application.

product of

BAXTER LABORATORIES, INC.

MORTON GROVE, ILLINOIS

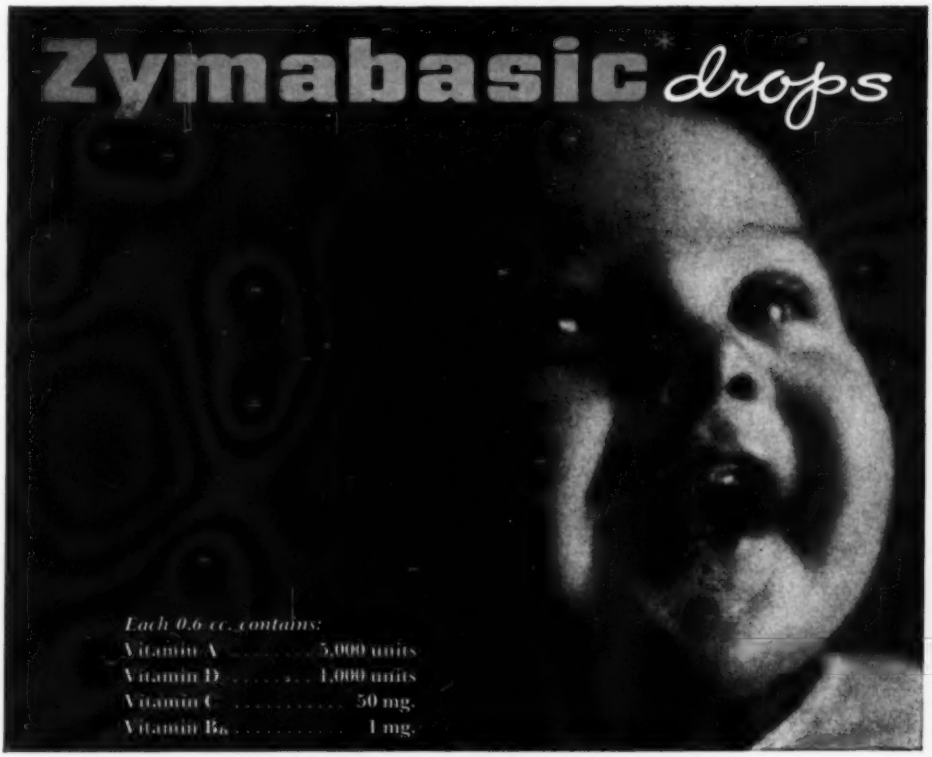
DISTRIBUTED AND AVAILABLE ONLY IN THE 37 STATES EAST OF THE ROCKIES (except in the city of El Paso, Texas) THROUGH

AMERICAN HOSPITAL SUPPLY CORPORATION

SCIENTIFIC PRODUCTS DIVISION GENERAL OFFICES • EVANSTON, ILLINOIS

80% of the A-D-C prescribers surveyed agreed that *basic* supplementation should include B_6 . . .

the "happy-baby vitamin"**



**Irritability, wakefulness, and regurgitation may be due to a deficiency of B_6.

Supplied: **15, 30, and 50 cc. dropper bottles**

Dosage: **0.3 cc. to 0.6 cc. daily**

*TRADEMARK

Upjohn

WANTED

RELIEF FROM ACNE

Fostex® *is an essential adjunct to treatment*

IN ACNE, Fostex Cream and Fostex Cake

- **degrease, peel and degerm the skin**
- **unblock pores . . . help remove blackheads**
- **help prevent pustule formation**
- **minimize spread of infection**

Fostex effectiveness is provided by Sebulytic® (sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate, sodium dioctyl sulfosuccinate) a new combination of surface active cleansing and wetting agents with remarkable antiseborrheic, keratolytic and antibacterial action, enhanced by sulfur 2%, salicylic acid 2% and hexachlorophene 1%.

Fostex is easy to use. The patient stops using soap on acne skin and starts washing with Fostex. Effective and well tolerated . . . assures patient acceptance and cooperation.

FOSTEX CREAM for therapeutic washing of the skin in the initial phase of the treatment of acne, when maximum degreasing and peeling are desired.

in 4.5 oz. jars

FOSTEX CAKE for maintenance therapy to keep the skin dry and substantially free of comedones.

in bar form

WESTWOOD PHARMACEUTICALS

Division of Foster-Milburn Co. **468 Dewitt Street** **Buffalo 13, New York**

for any child of any age in the vital first decade

The 'Deca-' Vitamin Family

three convenient dosage forms of 10 significant vitamins for comprehensive protection

is easy to specify because:

one basic name to remember—**'Deca-'**

one basic formulation

one standard of comprehensive protection

No refrigeration required • Special process assures stable B_{12} in solution with C • Hypoallergenic Unbreakable plastic 'Safti-Dropper' supplied with Deca-Vi-Sol

Deca-Mulcin®
Teaspoon dosage with delicious orange flavor

Deca-Vi-Caps®
Capsule dosage—small, easy-to-swallow capsules

Deca-Vi-Sol®
Dropper dosage with new, improved taste: "Best taste yet"

MEAD JOHNSON
SYMBOL OF SERVICE IN MEDICINE

DF532

The medication makes the big difference: Caldesene contains 15% calcium undecylenate for sustained antibacterial and antifungal action – Caldesene forms a protective coating which prevents moisture or other irritants from coming into contact with tender or affected areas. Since the film is discontinuous it does not interfere with insensible perspiration. This unique product relieves itching, soreness and burning, and protects against diaper rash, prickly heat, and chafing.

Supplied in 2 oz. shaker containers.

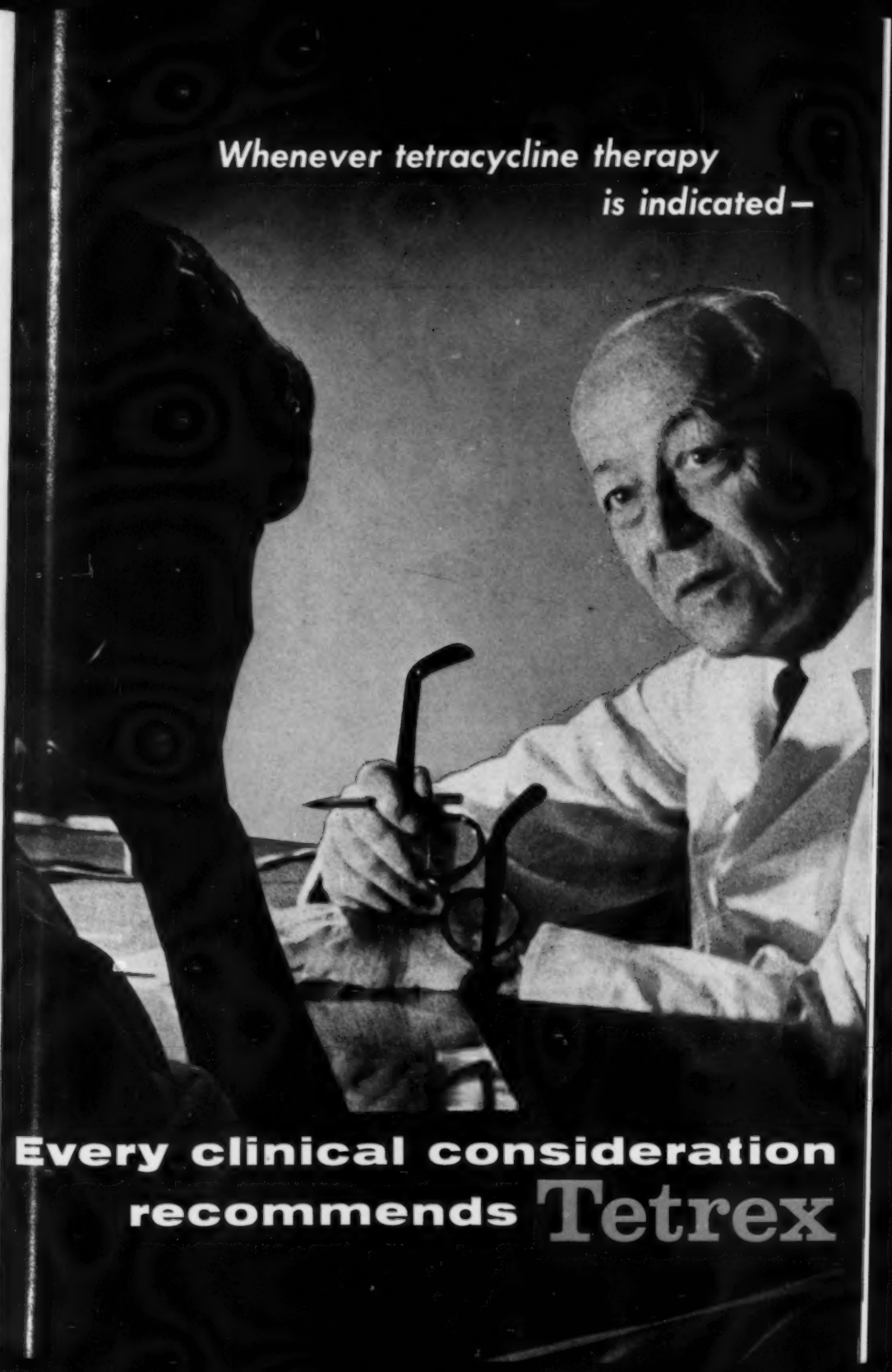
FOR A TRIAL SUPPLY WRITE TO
PROFESSIONAL SERVICE DEPARTMENT

Maltbie

MALTBIE LABORATORIES DIVISION
WALLACE & TIERNAN INC.

Belleville 9, New Jersey

PCD-71


Whenever tetracycline therapy is indicated—
Every clinical consideration recommends Tetrex

NOW...for the first time in tetracycline history!
significant
Tetrex
TETRACYCLINE PHOSPHATE COMPLEX
Bristol

24-hour blood levels

on a **SINGLE** intramuscular dose, in minimal injection volume

This achievement is made possible by the unique solubility of TETREX (tetracycline phosphate complex), which permits *more* antibiotic to be incorporated in *less* volume of diluent. Clinical studies have shown that injections are well tolerated, with no more pain on injection than with previous, less concentrated formulations.

TETREX Intramuscular '250' can be reconstituted for injection by adding 1.6 cc. of sterile distilled water or normal saline, to make a total injection volume of 2.0 cc. When the entire 250 mg. are to be injected, and minimal volume is desired, as little as 1.0 cc. of diluent need be used. (Full instructions for administration and dosage for adults and children, accompany packaged vial.)

Each one-dose vial of TETREX Intramuscular '250' contains:

TETREX (tetracycline phosphate complex) (tetracycline HCl activity).....**250 mg.**

Xylocaine* hydrochloride ..... **40 mg.**

plus ascorbic acid 300 mg. and magnesium chloride 46 mg. as buffering agents.

**® of Astra Pharm. Prod. Inc. for lidocaine*

SUPPLY: Single-dose vials containing TETREX — tetracycline phosphate complex — each equivalent to 250 mg. tetracycline HCl activity. Also available in 100-mg. single-dose vials.

INTRAMUSCULAR '250' WITH XYLOCAINE

BRISTOL LABORATORIES INC., SYRACUSE, NEW YORK

Every clinical consideration recommends

Tetrex®

THE ORIGINAL TETRACYCLINE PHOSPHATE COMPLEX

for faster, more certain control of infection

- A single, pure drug (not a mixture)
- High tetracycline blood levels
- Clinically "sodium-free"
- Equally effective, b.i.d. or q.i.d.
- Exceptionally free from adverse reactions
- Dosage forms for every therapeutic need

Bristol LABORATORIES INC., SYRACUSE, NEW YORK

Available for your prescription at all leading pharmacies

NEW ACHROMYCIN OPHTHALMIC OIL

TETRACYCLINE

SUSPENSION 1%

bland soothing drops

- floods tissues quickly, evenly
- compatible with ocular tissues and fluids
- eliminates cross contamination
- easily self-administered

supplied:

4 cc. plastic squeeze, dropper bottle containing ACHROMYCIN Tetracycline HCl (1%) 10.0 mg., per cc. suspended in sesame oil

unsurpassed in antibiotic efficacy

- Therapeutic: the true broad-spectrum action of ACHROMYCIN, promptly effective in a wide variety of common eye infections
- Prophylactic: following removal of foreign bodies; minor eye injuries
- Stable, no refrigeration needed: retains full potency for 2 years

LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY, PEARL RIVER, N. Y. Lederle

®Reg. U. S. Pat. Off.

For Fussy Patients

with finicky appetites

Whether 3 years, or seven, or in the difficult tween-age group...

Enriched Bread

can be of real help toward adequate nutrition when weight must be gained.

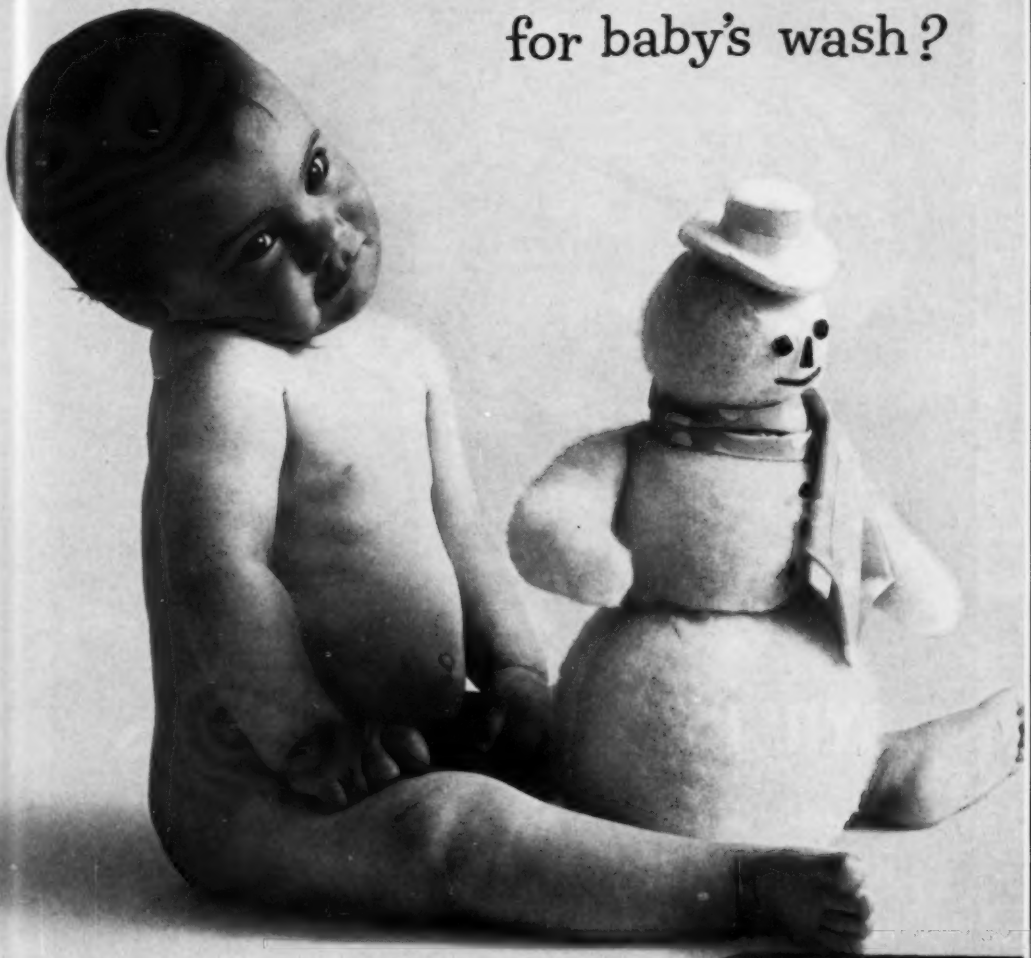
It is an excellent vehicle for other foods—foods which otherwise might be refused, and

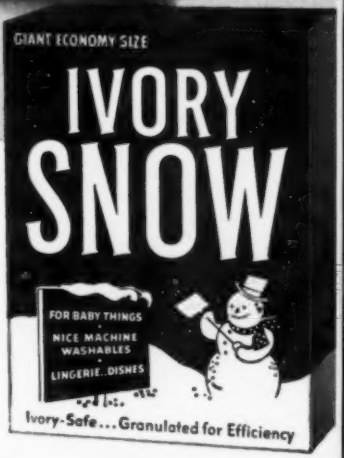
Itself makes a valuable contribution of growth-promoting protein, readily utilizable energy, B-vitamins, iron, and calcium.

AMERICAN BAKERS ASSOCIATION

20 North Wacker Drive • Chicago 6, Illinois

Why should you recommend Ivory Snow for baby's wash?



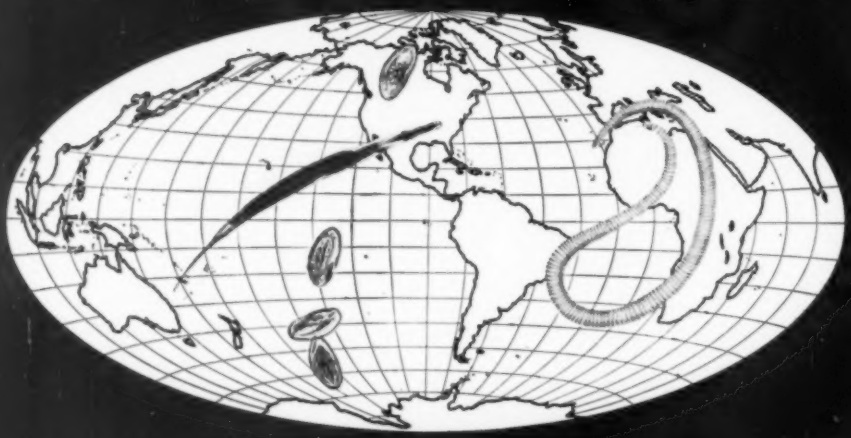


Because Ivory Snow is as safe and mild as soap can be . . . as pure a soap as mother can buy! Ivory Snow is Ivory-safe, leaves diapers and baby clothes soft, smooth...free from irritating deposits that can chafe tender skin. Granulated for washing machine efficiency, Ivory Snow is as practical for mother as it is safe for baby!

A Procter & Gamble Product

99 44/100% PURE® WITH BEAUTY GLOW

for "This Wormy World"



Pleasant tasting

'ANTEPAR'® brand

PIPERAZINE

SYRUP · TABLETS · WAFERS

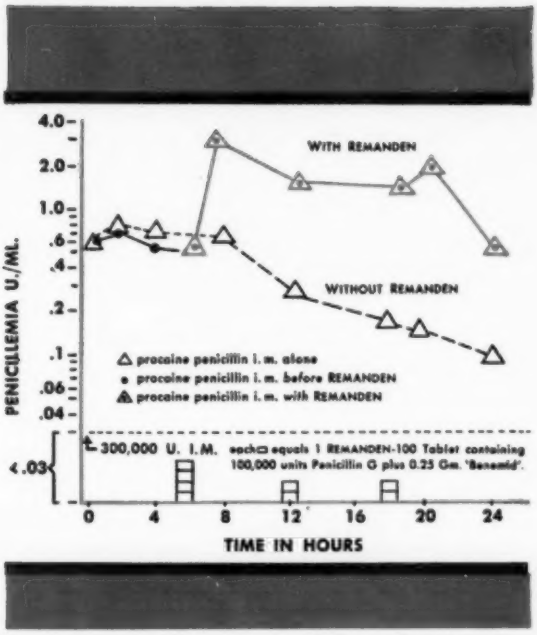
Eliminate **PINWORMS IN ONE WEEK**
ROUNDWORMS IN ONE OR TWO DAYS

PALATABLE · DEPENDABLE · ECONOMICAL

'ANTEPAR' SYRUP – Piperazine Citrate, 100 mg. per cc.
'ANTEPAR' TABLETS – Piperazine Citrate, 250 or 500 mg., scored
NEW **'ANTEPAR' WAFERS** – Piperazine Phosphate, 500 mg.

Literature available on request

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, N. Y.



The only oral penicillin that gives results comparable to parenteral penicillin

REMANDEN®

PENICILLIN WITH BENEMID®

The Benemid in REMANDEN allows recirculation of the penicillin—without interfering with normal renal function. Penicillin concentrations are 2 to 4 times higher with REMANDEN than with other oral penicillin preparations. Comparable, in fact, to those of intramuscular penicillin. REMANDEN can be used by itself or to supplement parenteral therapy. Available in Tablets or Suspension for flexible dosage.

MSD

MERCK SHARP & DOHME

DIVISION OF MERCK & CO., INC., PHILADELPHIA 1, PA

This advertisement conforms to the Code for Advertising of the Physicians' Council for Information on Child Health.

As with mother's milk . . .

Vitamins and Minerals

S-M-A contains all the vitamins and minerals
known to be required by normal infants—
in amounts more than adequate
to meet the recognized needs
of health and growth.
S-M-A is protected by
processing techniques that preserve
all these essential factors.

S-M-A®
Concentrated Liquid
Instant Powder

for sound infant nutrition

Wyeth®
Philadelphia 1, Pa.

This advertisement conforms to the Code for Advertising of the Physicians' Council for Information on Child Health.

As with mother's milk . . .

Carbohydrate

As with breast milk, S-M-A provides
true *physiological* carbohydrate
as the natural carbohydrate for infants.
S-M-A has no vegetable sugar.
Its only carbohydrate is lactose—
the sugar of milk. In amount also,
S-M-A carbohydrate (7%) is closely adjusted
to the average quantity in human milk.

S-M-A®

Concentrated Liquid
Instant Powder

Wyeth®
Philadelphia 1, Pa.

for sound infant nutrition

This advertisement conforms to the Code for Advertising of the Physicians' Council for Information on Child Health.

As with mother's milk . . .

Fatty Acids

Modern studies increasingly relate normal infant metabolism to the dietary content of essential unsaturated fatty acids. Like human milk, S-M-A fat is high in essential unsaturated fatty acids, and supplies in full the calories required of fat in the diet. Its fatty acid pattern closely parallels that of mother's milk.

S-M-A®

Concentrated Liquid
Instant Powder

for sound infant nutrition

Wyeth®
Philadelphia 1, Pa.

This advertisement conforms to the Code for Advertising of the Physicians' Council for Information on Child Health.

As with mother's milk . . .

Proteins

S-M-A contains 1.5 per cent protein,
and adequately satisfies
the baby's daily requirement
for protein.
The important elements in milk protein
are the amino acids. S-M-A agrees closely
with human milk in its content
of these essential substances.
S-M-A protein is complete and adequate.

S-M-A®
Concentrated Liquid
Instant Powder

for sound infant nutrition

Wyeth®
Philadelphia 1, Pa.

turn

spoon-spillers

into

angels

DELICIOUS

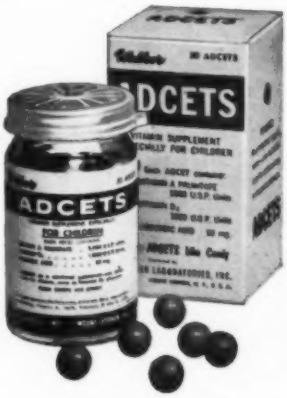
ADCETS®

orange-candy spheres of vitamins A, D and C

ADCETS are just the thing for chronic spoon-spillers—in fact they won't even suspect they are getting "medicine." ADCETS are *chewable* orange-flavored spheres of vitamins A, D and C.

Make vitamin time easy on patient *and* parents. Each sphere contains 5,000 U.S.P. units vitamin A palmitate, 1,000 U.S.P. units vitamin D_2, and 50 mg. ascorbic acid.

Bottles of 50 and 250.



Walker LABORATORIES, INC., MOUNT VERNON, N. Y., U. S. A.

"Functional vomiting

should be carefully distinguished from organic vomiting. Grave consequences may follow if evidences of organic derangement . . . are masked by treatment designed to control vomiting alone."[1]

SAFE

Safety First | in emesis therapy

Prescribe

EMETROL®

(Phosphorated Carbohydrate Solution) *First*

SAFE

EMETROL will not suppress symptoms arising from organic etiology. It controls vomiting of functional origin quickly.

Dosage: Adults, 1 or 2 tablespoonfuls; infants and children, 1 or 2 teaspoonfuls, as often as every 15 minutes. Always administer *undiluted*, and forbid oral fluids for at least 15 minutes after each dose. Even if first dose is not retained, continue administration. If vomiting is not controlled within one or two hours, look for organic etiology. For individual dosage regimens in various indications, please send for literature.

1. Bradley, J. E.: Mod. Med. 20 [illegible], No. [illegible], 1952.

SAFE

Kinney **KINNEY & COMPANY, INC.** Columbus, Indiana

MEAD JOHNSON

SYMBOL OF SERVICE IN MEDICINE

you can help ease the return to normal temperature

℞ **Tempra** | Drops Syrup

Acetaminophen, Mead Johnson

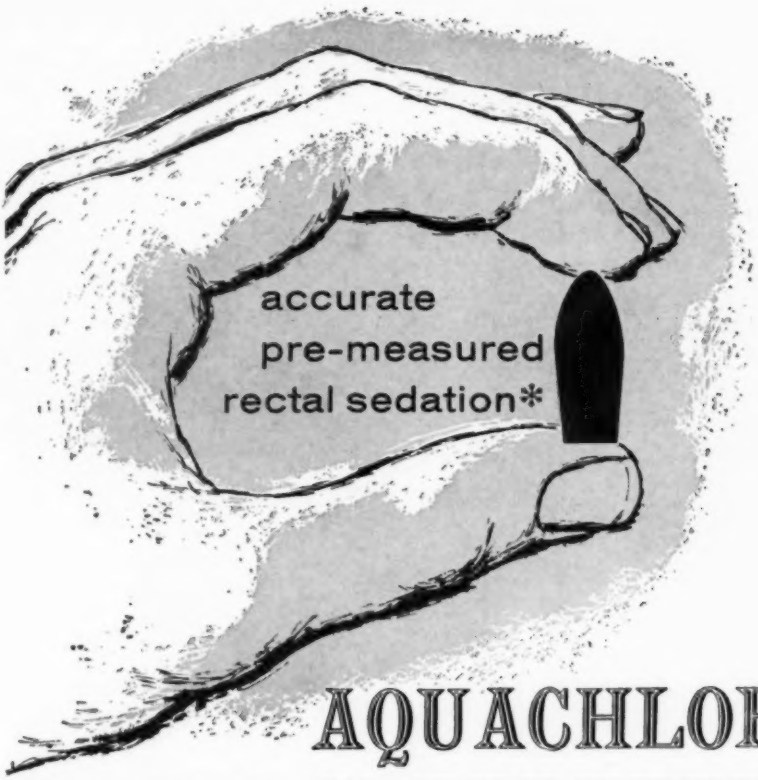
first physician-controlled antipyretic/analgesic in drop and teaspoon dosage forms

- easy to give, easy to take
- prompt and safe relief of fever, pain and discomfort
- on ℞ only—gives you better control of medication and dosage...gives parents added confidence

References on Acetaminophen:

(1) Goodman, L. S., and Gilman, A.: The Pharmacological Basis of Therapeutics, ed. 2., New York, The Macmillan Company, 1955, p. 313. (2) Batterman, R. C., and Grossman, A. J.: Fed. Proc. *14*:316, 1955. (3) Wallenstein, S. L., and Houde, R. W.: Fed. Proc. *13*:414, 1954. (4) Flinn, F. B., and Brodie, B. B.: J. Pharmacol. & Exper. Therap. *94*:76, 1948. (5) Mörner, K. A. H.: Ztschr. physiol. Chem. *13*:12, 1889. (6) Brodie, B. B., and Axelrod, J.: J. Pharmacol. & Exper. Therap. *94*:29, 1948. (7) Brodie, B. B., and Axelrod, J.: J. Pharmacol. & Exper. Therap. *97*:58, 1949. (8) Greenberg, L. A., and Lester, D.: J. Pharmacol. & Exper. Therap. *88*:87, 1946. (9) Smith, P. K., in Drill, V. A.: Pharmacology in Medicine, New York, McGraw-Hill Book Company, 1954, 21/1-4. (10) Lester, D., and Greenberg, L. A.: J. Pharmacol. & Exper. Therap. *90*:68, 1947.

TED25



AQUACHLORAL® SUPPRETTES®

CHLORAL HYDRATE
Rectally
SAFE SEDATION
WITHOUT HANGOVER

- Whenever oral therapy is difficult or impossible
- In nausea and vomiting
- To control convulsions
- To quiet hyperexcitability
- Preoperatively
- Postoperatively

The "Neocera" Base Makes the Difference

Contains no oils or fatty materials. Consists of water-soluble Carbowaxes* with active dispersal agent.
*Trademark U.C.C.

Aquachloral Supprettes give *total* drug release within 10 minutes after insertion for prompt sedation. Sedation is accomplished free of gastric or rectal irritation and barbiturate hangover. Rectal administration of Supprettes minimizes careless and excessive use. Dosage is non-cumulative.

Composition: Aquachloral Supprettes contain chloral hydrate in three dosage forms: 5 gr. (0.3 Gm.); 10 gr. (0.6 Gm.); 15 gr. (1.0 Gm.), in Webster's exclusive water-soluble "Neocera" dispersal base.

Supplied: In jars of 12.

Administration and Dosage: Rectally. *Children:* Under 2 years, 0.2 to 0.5 Gm.; 2–6 years, 0.5 to 1.0 Gm.; 6–12 years, 1.0 to 1.3 Gm. *Adults:* 0.6 to 1.2 Gm., as needed.

NO REFRIGERATION NECESSARY

SAMPLES ON REQUEST

Webster **THE WILLIAM A. WEBSTER COMPANY • MEMPHIS 5, TENNESSEE**

for a quick comeback

V-CILLIN, PEDIATRIC

(Penicillin V, Lilly)

patient-pleasing penicillin therapy

V-CILLIN, PEDIATRIC, 125—125 mg. per 5-cc. teaspoonful, in bottles of 40 and 80 cc.

V-CILLIN, PEDIATRIC, 250—250 mg. per 5-cc. teaspoonful, in bottles of 60 cc.

V-CILLIN DROPS—125 mg. per 0.6-cc. dropperful, in bottles of 1.5 Gm.

Also: 'V-Cillin-Sulfa' (Penicillin V with Triple Sulfas, Lilly), Pediatric—125 mg. 'V-Cillin' plus 0.5 Gm. triple sulfas per 5-cc. teaspoonful, in bottles of 60 cc.

'V-Cillin' assures maximum oral penicillin effectiveness and dependability: It is the only penicillin that passes through the stomach without loss of potency and is readily absorbed in the duodenum.

The normal acidity of the stomach, which rapidly destroys the soluble salts of penicillin G, has virtually no adverse effect on 'V-Cillin.'

Unlike the insoluble, poorly absorbed penicillin preparations, 'V-Cillin' is quickly and more completely absorbed.

ELI LILLY AND COMPANY • INDIANAPOLIS 6, INDIANA, U. S. A.

733166

end of the trail for old-time villains

In times past, the long-awaited debut of an infant upon life's stage was sometimes marred by the entrance of as beady-eyed, black-hearted villains as ever lurked in shadowy wings.

They were the digestive disturbances which occasionally beset the hungry baby for whom artificial feeding was prescribed.

Through the years, medical science worked on the problems of digestive disturbances in infants. Progress was gradually made, and then in 1929 leading clinicians demonstrated that evaporated milk offered one of the most versatile and satisfactory solutions to bottle feeding problems.

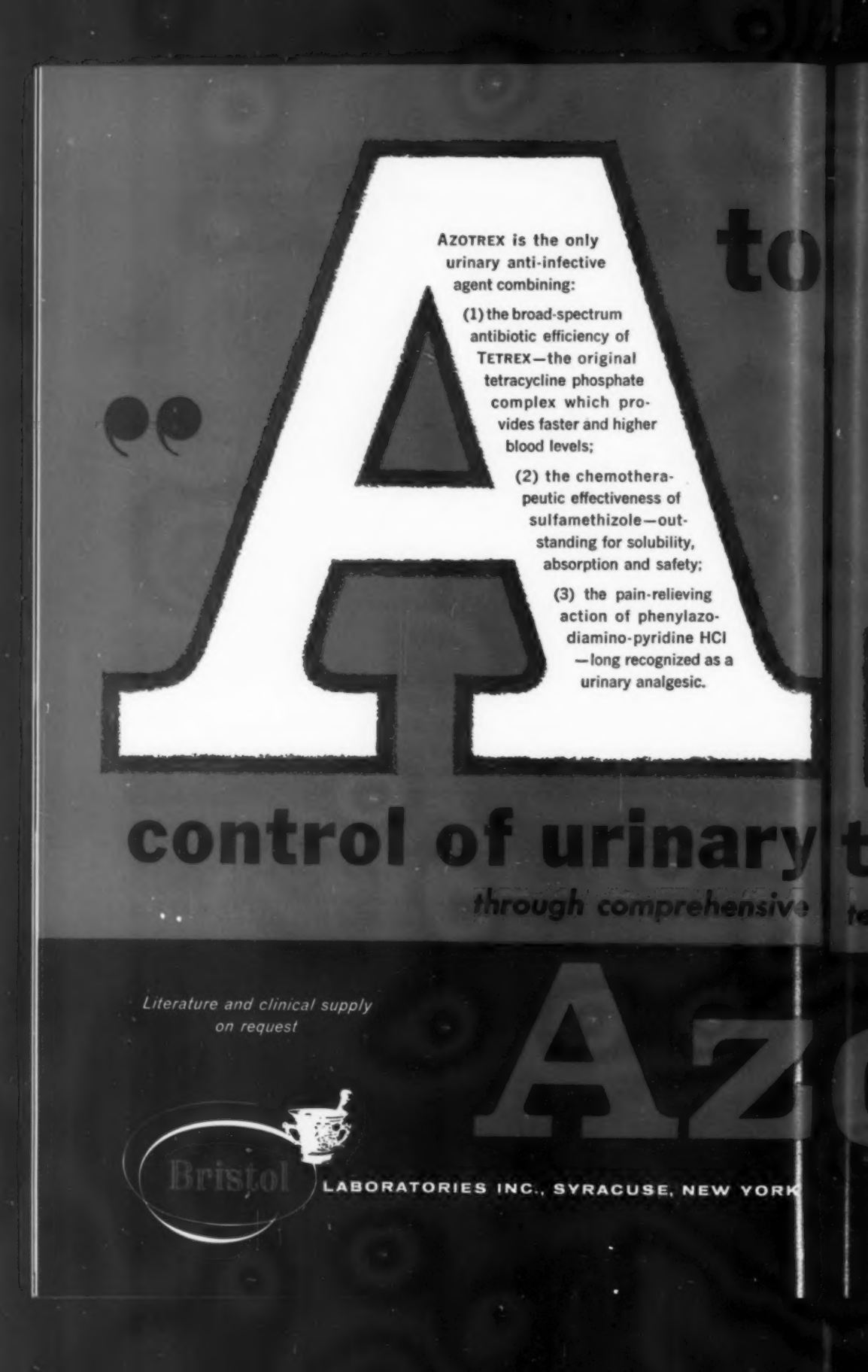
The old-time villains had been outwitted.

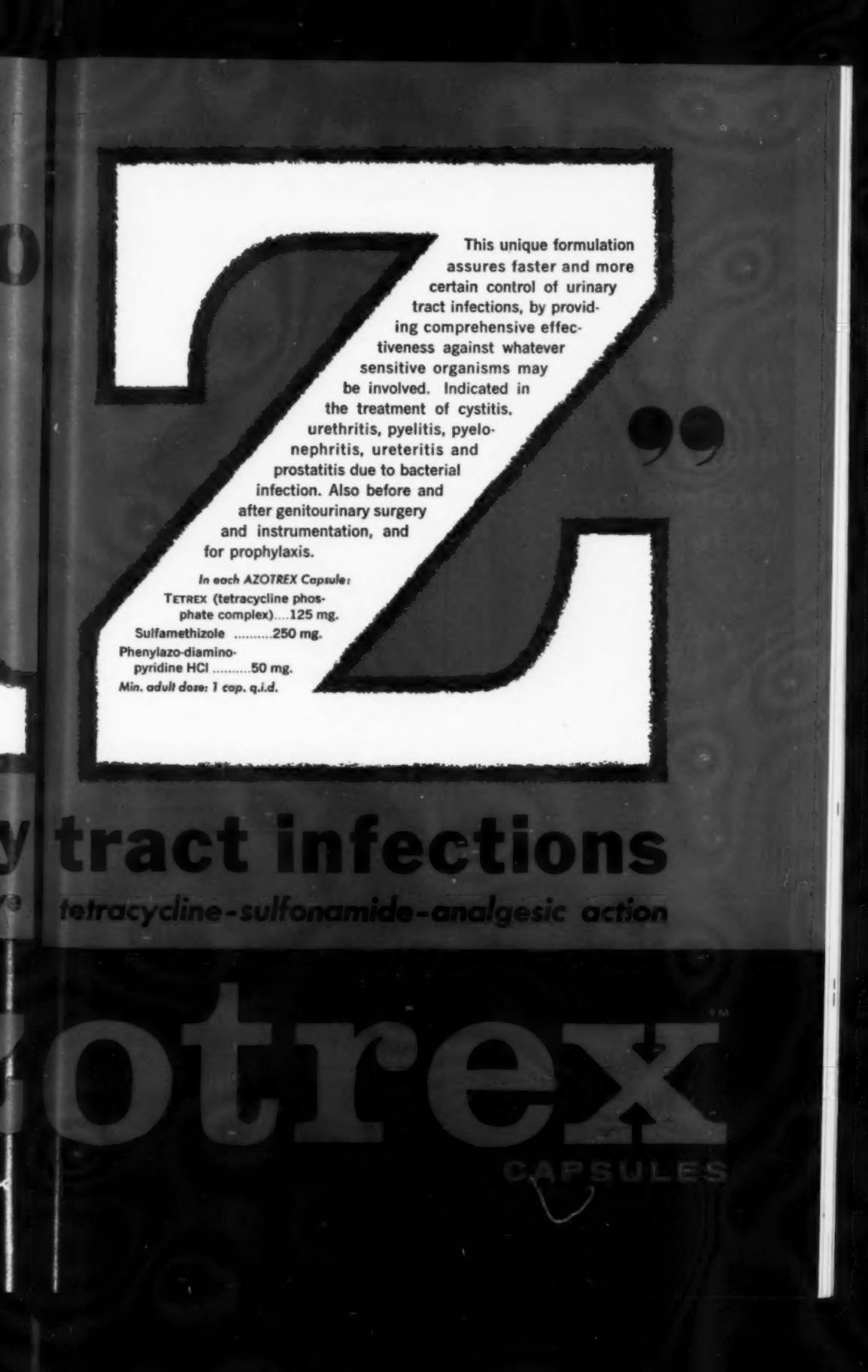
Since then, more than 50 million babies have been raised on evaporated milk.

Today, evaporated milk is still unique in its combination of advantages —a level of protein sufficient to duplicate the growth effect of human milk . . . flexibility in carbohydrate adjustment . . . easy digestibility . . . dependable sterility . . . *and* minimum cost.

PET EVAPORATED MILK . . . ***backed by 72 years of experience and continuing research***

PET MILK COMPANY • ARCADE BUILDING • ST. LOUIS 1, MISSOURI


AZOTREX is the only urinary anti-infective agent combining:
(1) the broad-spectrum antibiotic efficiency of TETREX—the original tetracycline phosphate complex which provides faster and higher blood levels;
(2) the chemotherapeutic effectiveness of sulfamethizole—outstanding for solubility, absorption and safety;
(3) the pain-relieving action of phenylazo-diamino-pyridine HCl—long recognized as a urinary analgesic.
control of urinary
through comprehensive
Literature and clinical supply on request
Bristol
LABORATORIES INC., SYRACUSE, NEW YORK


This unique formulation assures faster and more certain control of urinary tract infections, by providing comprehensive effectiveness against whatever sensitive organisms may be involved. Indicated in the treatment of cystitis, urethritis, pyelitis, pyelonephritis, ureteritis and prostatitis due to bacterial infection. Also before and after genitourinary surgery and instrumentation, and for prophylaxis.
In each AZOTREX Capsule:
TETREX (tetracycline phosphate complex)....125 mg.
Sulfamethizole .....250 mg.
Phenylazo-diamino-pyridine HCl .....50 mg.
Min. adult dose: 1 cap. q.i.d.
tract infections
tetracycline-sulfonamide-analgesic action
otrex
CAPSULES

in infantile eczema or diaper rash... avoid soap irritation... use

LOWILA® CAKE

The alkalinity of soap creates an environment favoring the growth of fungi and bacteria. Lowila is soap free . . . does not contain free alkali or any other irritating soap components. Lowila cleanses tender or dermatitic skin without irritation, maintains the normal acid mantle of the skin and creates an environment favorable to therapy and normal healing.

Write for samples Westwood PHARMACEUTICALS
Division of Foster-Milburn Company
468 Dewitt Street Buffalo 13, New York

SOAP IRRITATION WASTES SOUND DERMATOLOGIC THERAPY...RECOMMEND LOWILA

"ALL-NITE" MEANS WHAT IT SAYS... AND MORE!

NEW *Electresteem*
ALL-NITE VAPORIZER

Runs up to 16 hours without refilling

For relief of croup, cold and sinus congestions, *steam's* the thing! Electresteem provides it instantly, quietly, safely. All-Nite model *runs up to 16 hours without refilling!* Medication cup is king-size, too, for better than night-long operation. And you get king-size convenience with carrying stand, wide top opening which permits easy filling and cleaning, and other features. *One gallon* ALL-NITE *model,* $8.95. *Other Electresteem models from $3.95.*

- Vaporizes, deodorizes, humidifies
- Cool-handled carrying stand
- Pharmaceutical green glass bottle
- Automatic shut-off for extra safety

For information, write:
ELECTRIC STEAM RADIATOR CORPORATION
PARIS, KENTUCKY • Subsidiary of Landers, Frary & Clark

For

CONSTIPATED BABIES AND CHILDREN

softens stools by dietary means—promotes aciduric intestinal flora

NOW 2 FORMS

Specially processed non-diastatic barley malt extract neutralized with potassium carbonate.

LIQUID:
In 8 oz. and pt. jars.

POWDER:
In 8 oz. and 16 oz. jars. (use heaping measure)

Malt Soup Extract promotes growth of favorable aciduric intestinal flora and provides mild peristaltic stimulation. Safe, effective, non-habit forming—as confirmed by medical literature and clinical use for over 45 years.

FOR INFANTS: A gentle laxative modifier of milk. Just add one or two tablespoonfuls routinely to the day's formula, or in water for breast-fed infants. Prompt results, even in stubborn cases.

FOR CHILDREN: One or two tablespoonfuls with breakfast and at bedtime, by spoon or in milk. Makes a delicious "malted" drink.

SEND FOR SAMPLES

BORCHERDT CO.
217 N. WOLCOTT AVE., CHICAGO 12, ILL.

Synopsis of PEDIATRICS

by

JOHN ZAHORSKY, Professor Emeritus of Pediatrics and Director of the Department of Pediatrics, St. Louis University School of Medicine.

6th Ed. 470 pages, 158 illustrations. Published 1953. PRICE $7.50.

This book is a full treatise of the child—in sickness and in health. Every phase of child development and growth has been covered. Great pains were taken in this revision to incorporate the latest methods for the treatment of sick children.

A section on the medical emergencies in infants and children has been added to this edition. All procedures recommended are applicable to practice in the home or office.

THE C. V. MOSBY COMPANY,
3207 Washington Blvd.,
St. Louis 3, Missouri.

Date _____

Gentlemen: Send me the Sixth Edition of Zahorsky's "SYNOPSIS OF PEDIATRICS," priced at $7.50. ☐ Attached is my check. ☐ Charge my account.

Dr. _____ Street _____

City _____ Zone _____ State _____

PED-12-57

PROMINENT IN
The House Where Baby Lives

White's Vitamin A and D Ointment

When Baby's Skin Is Red and Sore—
topical A and D therapy promptly clears up diaper rash; prevents further irritation.

When Mama's Hands Are Rough and Raw—
from washing diapers or other household chores, a few applications eliminate "detergent dermatitis."

Also useful for—
routine nipple care, diabetic and varicose ulcers, bedsores, superficial wounds, abrasions, sunburn and minor burns.

Supplied: 1½ and 4 oz. tubes; 1 lb. jars and 5 lb. containers

WHITE Laboratories, Inc. Kenilworth, N.J.

SKIN PROTECTANT AGAINST DIAPER RASH

Also Protects Skin Against:
WOOL
PERSPIRATION
WEEDS
ALKALIES
SALIVA
SECRETIONS
ETC.

In 1 oz. tubes and 1 lb. jars
Send for sample and literature

Keep irritants away from skin with Silicote Skin Protectant Ointment. Frequent results between diaper changes! Not a drug; inert, adhesive, non-sensitizing. For the first time utilizing silicones—30% in petrolatum base.

ARNAR-STONE LABORATORIES, INC.
MOUNT PROSPECT, ILLINOIS

SILICOTE
SILICONE OINTMENT

Changing Your Address?

WHEN YOU MOVE, PLEASE—

(1) Notify us to change your address—allow us six weeks to make the change.
(2) Mention the name of this Journal. (We publish twelve periodicals.)
(3) Give us your old address. If possible, return the addressed portion of the envelope in which we sent your last copy.
(4) Give us your new address—complete—including the Postal zone number.
(5) Please print your name and address.

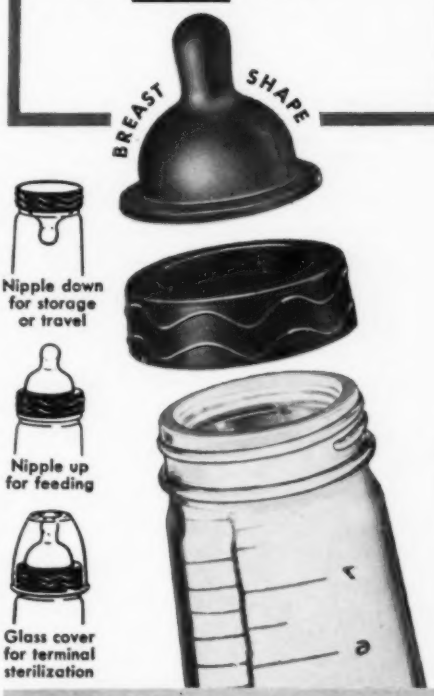
Thank You!

Circulation Department, The C. V. Mosby Company, Publishers, 3207 Washington Blvd., St. Louis 3, Mo.

HYGEIA ...the MOST HYGIENIC Nurser

used by more hospitals than any other nationally-advertised nurser . . .

NOW AVAILABLE IN SCREW-CAP BOTTLES FOR HOME USE



Larger "Breast-Shape" Nipple prevents baby's lips from touching unsterile ring—avoids malformation of jaw caused by constant pressure against hard plastic ring.

Positive Flow Control by adjusting screw cap. Air vent channels can't clog; no pinholes to clean.

Shorter Nipple Tip delivers formula in forepart of mouth to mix readily with digestive juices—helps prevent gagging because nipple does not touch uvula.

Easy to Push Nipple Through Ring to feeding position without contaminating nipple with fingers.

Easiest to Keep Sanitary: no corners to collect dried formula — nipple can be turned inside out for scrubbing. Widest mouth — easiest to clean and fill bottle.

Red Measurement Scale — easier to read at a glance.

SEND FOR *FREE* SAMPLE!

BALL BROTHERS COMPANY
Consumer Products Drug Division, Dept. JP 7
Muncie, Indiana

Please send sample Hygeia Screw-Cap Nurser and literature.

Dr.....
Street.....
City and State.....

©1956 B. B. CO.

SERVING THE MEDICAL PROFESSION SINCE 1894

ALLERGY in PEDIATRIC PRACTICE

by

WILLIAM B. SHERMAN, M.D., Associate Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons; Associate Attending Physician, Presbyterian Hospital; Attending Physician, Roosevelt Hospital, New York, New York; and **WALTER R. KESSLER, M.D., Ph.D.**, Instructor in Pediatrics, Columbia University, College of Physicians and Surgeons; Assistant Pediatrician, Babies Hospital; Assistant Attending Physician, Roosevelt Hospital, New York, New York.

300 Pages—Illustrated—Price $9.25

Here is practical aid in the diagnosis and treatment of infants and children suffering from allergic diseases. A certain amount of basic scientific background is included for the intelligent use by general practitioners and pediatricians without special training in allergy.

It presents in detail the views and methods which have been found most useful in actual practice. When controversial problems are discussed the authors indicate the differences of opinion and differentiate fact from theory. However, the desire to keep the book simple and practical does not permit detailed and impartial presentation of all points of view on controversial problems. Attention is focused on those diseases in which allergic methods of diagnosis and treatment have proved of real, practical value.

Since the book is intended for practitioners without special training in the field of allergy, it seems safe to assume that this information is either new to them or long since forgotten. The citation of references to other publications is intended to indicate relatively few sources from which more detailed information and bibliographies may be obtained. In most cases these are review articles or books rather than original sources.

Order today from

THE C. V. MOSBY CO.

3207 Washington Blvd.
St. Louis 3, Mo.

Date _____

THE C. V. MOSBY COMPANY
3207 Washington Blvd.
St. Louis 3, Missouri

Gentlemen: Send me Sherman-Kessler "ALLERGY IN PEDIATRIC PRACTICE." Price $9.25.

☐ Charge my account ☐ Attached is my check

Dr. _____

Street _____

City _____

Zone _____ State _____

PED-12-57

NEW...

A more potent, more effective, lower-dose antidiarrheal

With a powerful new adsorbent—having five times the adsorbent action of kaolin

With two synergistic antibiotics—having a more effective antidiarrheal spectrum (with systemic absorption so minimal as to preclude toxicity)

With increased potency—for greater therapeutic effectiveness, smaller dose

With refreshing taste—for acceptability in all age groups

Supplied: Bottles of 8 fl. oz.

Polymagma*

Wyeth

Philadelphia 1, Pa.

*Trademark

THE JOURNAL OF PEDIATRICS

EDITOR

BORDEN S. VEEDER, M.D., 3207 Washington Blvd., St. Louis 3, Mo.

PUBLISHED BY THE C. V. MOSBY COMPANY, 3207 WASHINGTON BLVD.
ST. LOUIS 3, MO., U. S. A.

Entered at the Post Office at St. Louis, Mo., as Second Class Matter.

Published Monthly. Subscriptions may begin at any time.

Editorial Communications

Original Communications.—Manuscripts for publication and correspondence relating to them should be sent to Dr. Borden S. Veeder, 3207 Washington Blvd., St. Louis 3, Mo., U. S. A. Articles are accepted for publication upon the understanding that they are contributed solely to The Journal of Pediatrics.

Manuscripts should be typewritten on one side of the paper only, with double spacing, and liberal margins. References should be placed at the end of the article and should include, in the order given, name of author, journal, volume, page and year; e.g., Smith: J. Pediat. 1: 10, 1952. Journal abbreviations as used in the publications of the American Medical Association should be followed. Illustrations accompanying manuscripts should be numbered, provided with suitable legends, and marked lightly on back with author's name. Articles accepted for publication are subject to editorial revision.

Neither the editors nor the publishers accept responsibility for the views and statements of authors as published in their communications.

Illustrations.—A reasonable number of half-tone illustrations will be reproduced free of cost to the author, but special arrangements must be made with the editor for color plates, elaborate tables or extra illustrations. Copy for zinc cuts (such as pen drawings and charts) should be drawn and lettered only in India ink, or black typewriter ribbon (when the typewriter is used), as ordinary blue ink or colors will not reproduce. Only good photographic prints or drawings should be supplied for halftone work.

Books for Review.—Only such books as are considered of interest and value to subscribers will be reviewed, and no published acknowledgment of books received will be made. These should be sent to Dr. Borden S. Veeder, 3207 Washington Blvd., St. Louis 3, Mo.

Reprints.—Reprints of articles must be ordered specifically, in separate communication to the publishers, The C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, Mo., who will send their schedule of prices. Individual reprints of an article must be obtained through the author.

Business Communications

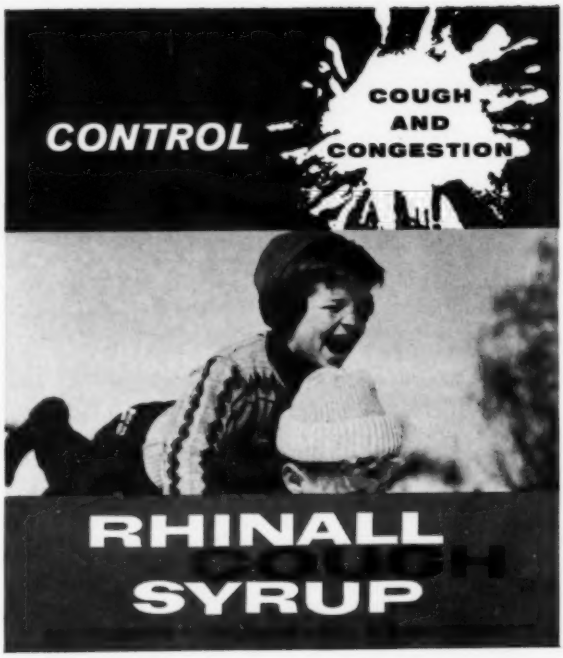
Business Communications.—All communications in regard to advertising, subscriptions, change of address, etc., should be addressed to the publishers, The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Mo.

Subscription Rates.—United States and its Possessions $12.00, Students $6.00; Canada, Latin-America, and Spain $13.00, Students $7.00; Other Countries $14.00, Students $8.00. Single copies, $2.00 postpaid. Remittances for subscriptions should be made by check, draft, post office or express money order, payable to this Journal.

Change of Address Notice.—Six weeks' notice is required to effect a change of address. Kindly give the exact name under which a subscription is entered, and the full form of both old and new addresses, including the post office zone number.

Advertisements.—Only articles of known scientific value will be given space. Forms close first day of month preceding date of issue. Advertising rates and page sizes on application.

Bound Volumes.—Publishers' Authorized Bindery Service, 5811 West Division Street, Chicago 51, Illinois, will quote prices for binding complete volumes in permanent buckram.



Specific antitussive action of Narcotine affords selective control of the cough reflex.

- non-toxic
- non-habit forming
- free from side effects

RHINALL COUGH SYRUP

makes cough more productive

soothes bronchial irritation

Supplied: 3 oz. and pint bottle. Exempt Narcotic

Each 5 cc. teaspoonful contains:

Narcotine	5.0 mg.
Phenylephrine Hydrochloride	5.0 mg.
Pyrilamine Maleate	12.5 mg.
Glyceryl Guaiacolate	50.0 mg.
Citric Acid	50.0 mg.
Sodium Citrate	22.5 mg.
Alcohol	5.0%

RHINOPTO COMPANY - Dallas, Texas

---

when perianal irritations develop

- **SOOTHING FOR BABY**
- **CONVENIENT FOR MOTHER**

In diaper rash, diarrhea and prickly heat Tucks are especially convenient for cleansing and as a hygienic aid. They are cooling and soothing to the irritated surface. Tucks are simple, economical and convenient for mother and may be used in conjunction with specific medication.

Tucks

—SOFT PADS MOISTENED WITH WITCH HAZEL AND GLYCERIN; ECONOMICAL AND DISPOSABLE IN TOILET

For these frequently occurring irritations, recommend to the mother that Tucks be used and kept on hand.

Simply print your name and office address in this space and send to us. You will receive four complimentary trade packages of Tucks for use with four patients.

NAME _____

ADDRESS _____

CITY _____ STATE _____

fuller PHARMACEUTICAL COMPANY • MINNEAPOLIS 16, MINNESOTA

Canadian Distributor: WINLEY-MORRIS COMPANY, Ltd. 6579 Somerled Avenue, Montreal

Articles to appear in early issues of

The JOURNAL OF PEDIATRICS

Blood Pressure Studies in Infants and Children With an Electric Microphone.
By Robert K. Endres, M.D., David Goldring, M.D., and M. Remsen Behrer, M.D., St. Louis, Mo.

An Analgesic Mixture for Minor Surgical Procedures in Young Children.
By Fred N. Mitchell, M.D., and George R. Minor, M.D., Charlottesville, Va.

The Incidence of Allergic Disease in the General Practice of Pediatrics.
By William G. Crook, M.D., Walton W. Harrison, M.D., and Stanley E. Crawford, M.D., Jackson, Tenn.

Lysine Tolerance in Infants.
By E. Dubow, M.D., A. Maher, M.S., D. Gish, Ph.D., and V. Erk, M.D., New York, N. Y.

The Antibody (Hemagglutinin) Response as a Tool for Etiologic Diagnosis of Diarrheal Disease.
By E. Neter, M.D., and L. Suskind, M.D., Buffalo, N. Y.

The A-B-O Blood Groups in Relation to Prematurity and Stillbirth.
By Stanley Alan Plotkin, M.D., Cleveland, Ohio.

Observations on the Plasma Lipoproteins in a Case of Tay-Sachs Disease.
By Harold W. Dargeon, M.D., Marion Barclay, Ph.D., D. Nackie Calathes, B.S., and Marilyn J. Brownell, B.A., New York, N. Y.

Addison's Disease in Children.
By Robert E. Greenberg, M.D., Detroit, Mich.

Sucrosuria in Association With Mental Deficiency and Hiatal Hernia.
By Gerald G. Woodruff, Jr., M.D., London, England.

Megimide in the Treatment of Severe Barbiturate Poisoning.
By Brian E. Nolan, M.D., Springfield, Ill.

Malathion Poisoning in a 34-Month-Old Child Following Accidental Ingestion.
By Herbert Goldman, M.D., and Maurice Teitel, M.D., Manhasset, N. Y.

The Relation of Pectus Excavatum to Pectus Carinatum.
By Charles W. Lester, M.D., New York, N. Y.

An Objective Survey of Dental Malocclusions in Children.
By Berman S. Dunham, M.D., Toledo, Ohio.

Speech Problems in Children.
By Irwin Lehrhoff, Ph.D., Torrance, Calif.

Reflections on Infantile Gastroenteritis and Its Treatment.
By S. Levin, M.B. (Rand), M.R.C.P.(Edin) D.C.H., Johannesburg, South Africa.

Acute Appendicitis in Early Childhood.
By Francesco Minervini, M.D., and Thomas V. Santulli, M.D., New York, N. Y.

A Study of Pathology of Stillbirths and Neonatal Deaths in South India.
By G. G. Hadley, E. W. Gault, and M. D. Graham, Vellore, South India.

The Neck-Righting Reflex in Children.
By Robert L. Spitzer, M.D., Yale Kramer, M.D., and Richard Rabkin, M.D., New York, N. Y.

In contrast to proprietary formulas, which can only be made weaker or stronger, the evaporated milk formula is *flexible* because it can be:

– adjusted in dilution and *carbohydrate content* to meet neonatal needs without renal overload.

– gradually increased in concentration and the carbohydrate *specified by the physician* as the baby grows.

– adjusted in concentration, nutritional balance, or both, in any period of stress, such as illness.

– decreased in carbohydrate in direct ratio with the infant's increasing ability to assimilate solid foods.

– used in place of fresh milk at normal milk dilution during weaning from bottle to cup.

Carnation

"FROM CONTENTED COWS"

Optimum prescription-quality in today's trend to the individualized formula.

The October, 1957 Issue

of the

JOURNAL of CHRONIC DISEASES

A Symposium

The Management of Hematologic Disorders

Special Editors

MAXWELL M. WINTROBE, M.D. **CARL V. MOORE, M.D.**

INTRODUCTION TO SYMPOSIUM ON THE MANAGEMENT OF HEMATOLOGIC DISORDERS. MAXWELL M. WINTROBE, M.D., PH.D., SALT LAKE CITY, UTAH, AND CARL V. MOORE, M.D., ST., LOUIS, MO. 285

TREATMENT OF MEGALOBLASTIC ANEMIAS. PATRICIA A. MCINTYRE, M.D., JULIUS R. KREVANS, M.D., AND C. LOCKARD CONLEY, M.D., BALTIMORE, MD. 287

TREATMENT OF IRON DEFICIENCY ANEMIA IN THE ADULT. G. PIRZIO-BIROLI, M.D., AND CLEMENT A. FINCH, M.D., SEATTLE, WASH. 302

TREATMENT OF HEMOLYTIC DISORDERS. LAWRENCE E. YOUNG, M.D., GERALD MILLER, M.D., AND SCOTT N. SWISHER, M.D., ROCHESTER, N. Y. 307

THE TREATMENT OF REFRACTORY ANEMIA OF BONE MARROW FAILURE. CARL V. MOORE, M.D., ST. LOUIS, MO. 324

THE TREATMENT OF POLYCYTHEMIA VERA. EDWARD H. REINHARD, M.D., AND BETTY HAHNEMAN, M.D., ST. LOUIS, MO. 332

THE TREATMENT OF INFECTIOUS MONONUCLEOSIS. BRUCE K. WISEMAN, M.D., COLUMBUS, OHIO 347

LEUKOPENIA: ITS MECHANISM AND THERAPY. JOHN S. LAWRENCE, M.D., LOS ANGELES, CALIF. 351

THERAPY OF THE PURPURAS. WILLIAM J. HARRINGTON, M.D., ST. LOUIS, MO. . . . 365

THE THERAPY OF DISORDERS OF COAGULATION. MARTIN C. ROSENTHAL, M.D., NEW YORK, N. Y. 383

THE RELATIVE FREQUENCY OF THE SEVERAL TYPES OF CHRONIC LEUKEMIA AND THEIR MANAGEMENT. FRANK H. BETHELL, M.D., ANN ARBOR, MICH. 403

THERAPY OF ACUTE LEUKEMIA IN ADULTS. ROSE RUTH ELLISON, M.D., AND JOSEPH H. BURCHENAL, M.D., NEW YORK, N. Y. 421

SOME ASPECTS OF THE LYMPHOMA PROBLEM. LEON O. JACOBSON, M.D., CHICAGO, ILL. 437

THE MANAGEMENT OF MULTIPLE MYELOMA. WILLIAM S. ADAMS, M.D., AND WILLIAM A. SKOOG, M.D., LOS ANGELES, CALIF. 446

Copies of the Symposium Issue Are Available—See Order Form, Below

---------- ORDER FORM ----------

THE C. V. MOSBY CO., 3207 Washington Blvd., St. Louis 3, Mo., U.S.A.

Dear Sirs: —Send me the HEMATOLOGIC DISORDERS symposium issue, for $2.00 —Enter my subscription to the JOURNAL OF CHRONIC DISEASES, for $12.50 (International Postage, Canada & Latin America, $0.50; Elsewhere, $1.50), and send the SYMPOSIUM ISSUE, and the November and December issues, free.

—I am enclosing $_____ —Bill me for $_____

Dr. _____
Number & Street

City _____
Post Office Zone State or Province

air
in
a
hurry

+

protection
from asthma
for hours
with 1
convenient tablet—

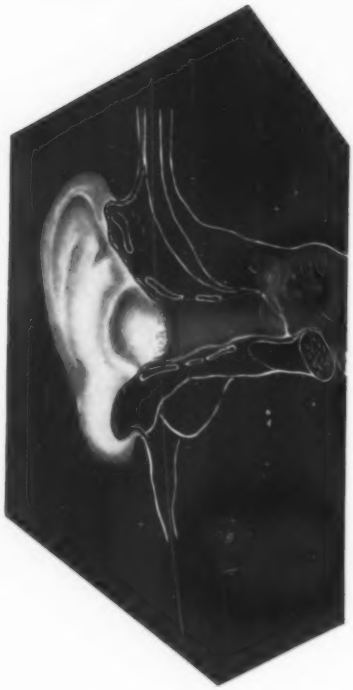
Nephenalin®
PEDIATRIC

each tablet contains:

Aludrine (Isoproterenol HCl)	5 mg. (in coating)
plus	
Theophylline	100 mg. (1½ gr.)
Ephedrine sulfate	12 mg. (3/16 gr.)
Phenobarbital	8 mg. (1/8 gr.)

dose: Keep under tongue 5 minutes for rapid asthma relief; then swallow. Not more than 1 tablet in 4 hours, or 5 tablets per day. Bottles of 20 and 100.

Thos. Leeming & Co. Inc. New York 17, N. Y.



Cleansing chemotherapy
in external ear infections

otomide®

Eliminates:
Sulfa-Susceptible Pathogens
Infected Tissue Debris
Foul Odors

Formula:

Urea (carbamide)	10%
Sulfanilamide	5%
Chlorobutanol (anhydrous)	3%
Glycerin (high specific gravity)	q.s.

In 15 cc. dropper bottles.

White Laboratories, Inc., Kenilworth, N. J.

How to pep up a poor appetite

REDISOL®

CYANOCOBALAMIN (CRYSTALLINE VITAMIN B_{12})

When REDISOL—pure vitamin B_{12}—is used as a dietary supplement, weight gain and increase in appetite often follow. The cherry-flavored Elixir and soluble Tablets dissolve readily in liquids.

MSD

MERCK SHARP & DOHME
DIVISION OF MERCK & CO., INC., PHILADELPHIA 1, PA.

for "earache"
and "itching" ears

otodyne®...

Otodyne brings gratifying symptomatic relief in simple "earache" and in pruritic conditions of the external ear canal.

Quick-acting Zolamine (1%) and long-acting Eucupin® (0.1%) are combined in a polyethylene base which does not obscure anatomic landmarks.

In 15 cc. dropper bottles.

White Laboratories, Inc.
Kenilworth, N. J.

"Doing what comes naturally..."

From "start" to six years, wearing Self-Starters is the nearest thing to going barefoot. Though properly protective, they're so completely flexible and provide so much toe-room that, as the child stands, walks, runs, jumps (and relaxes) they give every bone and muscle full play to function, grow and develop *naturally* . . . thus laying the foundation for lifelong foot health and comfort.

That's why so many pediatricians approve of Self-Starters. To learn why they are ideal "start to six" shoes for normal feet, write today for descriptive literature and name of nearest experienced fitter.

THE CARPENTER SHOE COMPANY, INC.
161 CLARISSA STREET, ROCHESTER 8, N. Y.

Self-Starters
BY CARPENTER

Mr. Louis C. Weld, President of G. W. Chesbrough Co., demonstrates straight last, rigid sole of Cosyfoot surgical. Will not buckle or warp in splint.

These corrective pre-walkers will help you and your patients

Big promise? Maybe. But here's why I think it's safe to say this new line of high-grade but *moderately* priced corrective pre-walkers offers you an opportunity. You can prescribe them with confidence and know your patients will not be overcharged.

A while ago a child in my own family needed a corrective shoe. I discovered then what a hardship the expense of most corrective footwear can mean to parents.

That's when we got busy in our Cosyfoot plant and put all our 58 years of experience into the shoes you see here: Corrective pre-walkers—moderately priced!

Use with or without Denis Browne splints, and to hold correction after removal of casts. The coupon will bring you a trial pair.

OUTSIDE COUNTER

No. 1700 Club Foot Pre-Walker. Meets strict orthopedic specifications. Heel stabilizer instep strap. Open toe.

NO BACK SEAM

Open toe surgical Pre-Walker. Straight line symmetrical last, firm heel. Steel plate between insole and outsole for rigidity. **No. 1400**

PERFECTLY SMOOTH INSIDE

No. 1300 Closed toe surgical Pre-Walker. Lace-to-toe design permits snug, gentle fit. Unlined construction allows upper to breathe.

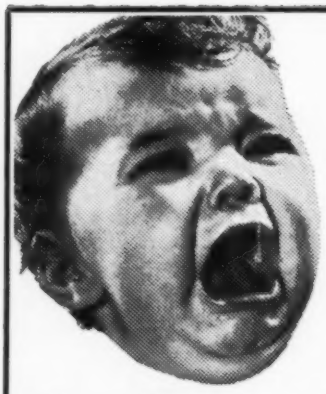
MAIL COUPON now for free desk sample.

G. W. CHESBROUGH, INC.
799 SMITH STREET • ROCHESTER 6, N. Y.

NAME.....

ADDRESS.....

CITY.....



Stop diaper rash before it starts . . .

Used in diaper pail and in daily washing

•

No special rinse needed

Eliminates boiling and bleaching! Ends use of borax, and quaternary ammonia rinses!

At all drug and food stores

1 package washes and treats 300 diapers.

ACTIVE INGREDIENTS:
Tri-Ethyl-Methol-Azurine-Oleate 5%
Boro-Meta-Phos. 37%

Physicians' samples on request

CENTRAL DRUG
1392 Niagara St. Buffalo 13, N. Y.

Handbook of
PEDIATRIC MEDICAL EMERGENCIES

by

ADOLPH G. DeSANCTIS, M.D., Professor of Pediatrics and Chairman of the Department of Pediatrics, Post-Graduate Medical School, New York University-Bellevue Medical Center. With the Collaboration of CHARLES VARGA, M.D., Portland, Oregon.

Second Edition. 389 pages, 73 illustrations. PRICE, $6.25.

Childhood diseases and accidents call for rapid, emergency therapy in almost every case—and the Pediatrician or General Practitioner (into whose hands the majority of these calls fall first) will find practical, clinical information in this book.

Originally prepared for use by the resident staff and for physicians enrolled in the courses offered by the Pediatric Department of the Post-Graduate Medical School at New York University–Bellevue Medical Center, this book has been expanded to make it even more practical and useful.

Much of the text has been completely rewritten and new illustrations and tables have been added. The chapters on Metabolic Emergencies, Accident and Poison Prevention, Genitourinary Emergencies, Respiratory Paralysis in Poliomyelitis are new. Additions have been made to the list of household poisons.

Contents: Cardiovascular Emergencies. Metabolic Emergencies. Genitourinary Emergencies. Neurological Emergencies. Respiratory Emergencies. Respiratory Paralysis in Poliomyelitis. Care of the Premature Infant. Miscellaneous Emergencies. Pediatric Procedures. Drowning. Accident and Poison Prevention. Poisoning. Appendix.

Comment of Reviewer for GP

"This is a valuable quick reference handbook for both pediatricians and general practitioners. It should be within easy reach of every physician who has children patients.

"The book is not intended as a complete pediatric textbook, but in the field of emergency treatment it is unexcelled. Especially valuable are the sections on poisoning, drowning, and convulsions. Although the book is based upon hospital experience, it contains much that should be of value to the general practitioner caring for cases in the home. Dr. DeSanctis and his associates have produced a volume which will be widely used and be the means of saving many lives."

THE C. V. MOSBY COMPANY
3207 Washington Blvd.
St. Louis 3, Missouri

Date _____

Gentlemen: Send me the Second Edition of DeSanctis-Varga "HANDBOOK OF PEDIATRIC MEDICAL EMERGENCIES," priced at $6.25. ☐ Attached is my check. ☐ Charge my account.

Dr. _____ Street _____

City _____ Zone _____ State _____

PED-12-57

Integrated and
ENTIRELY NEW!

PRACTICE
of
MEDICINE

Edited By

JONATHAN CAMPBELL MEAKINS

1,916 Pages. 318 Illus. 4 in Color. 6th Ed.
Price, $16.00.

Except for the title there is very little similarity between this enlarged and expanded edition of "PRACTICE OF MEDICINE" and the five previous editions. Where the first five editions were almost entirely the work of Doctor Meakins, he has served only as Editor-in-Chief of this edition. Working under him were 24 Associate Editors—and they, in turn, had 87 contributors do most of the actual writing. As a result the book is entirely new and different.

Designed to assist the practitioner of medicine in solving the numerous puzzles and problems which he daily encounters, this book is arranged according to diseases of the various systems and organs—a plan that lends itself to simplicity. It is eminently a clinical book with symptoms being given particular prominence. The pathological basis of symptoms is everywhere stressed, and the bedside recognition and interpretation of clinical signs is described with a sustained interest and lucidity rarely found in tomes of this size.

In each section where applicable, reference to the so-called psychosomatic patterns and psychologic aspects has been made, and there is, finally, a section on Psychosomatic Medicine, designed to knit the general concepts of this branch into an integrated whole.

THE C. V. MOSBY COMPANY Date_____
3207 Washington Blvd.
St. Louis 3, Missouri

Gentlemen: Send me Meakins "PRACTICE OF MEDICINE," priced at $16.00. ____Attached is my check (Postage Paid). ____Charge my account, plus postage.

Dr. _____

Street _____

City _____ Zone ____ State _____

PED-12-57

SUPERIOR TOLERANCE

"Of the 75 patients receiving iron [MOL-IRON] therapy, [only] one was forced to stop treatment . . ."

(Am. J. Obst. & Gynec. 62:947, Nov. 1951.)

OUTSTANDING EFFECTIVENESS

"We have never had other iron salts so efficacious . . ."

(Am. J. Obst. & Gynec. 57:541, Mar. 1949.)

RAPID RESPONSE

". . . produced a substantially more rapid therapeutic response than ferrous sulfate . . ."

(Bull. Margaret Hague Mat. Hosp. 1:68, Sept. 1948.)

these are the hallmarks of

MOL-IRON®

(Molybdenized Ferrous Sulfate)

and it costs no more
than ordinary
iron preparations

The outstanding therapeutic advantages of Mol-Iron have been established by more published clinical reports[1-14] during the past ten years, than are available for any other iron preparation.

Complete bibliography available on request.

there is a specific

MOL-IRON®

(MOLYBDENIZED FERROUS SULFATE)

preparation to fit each patient's need

For simple iron-deficiency anemia—

MOL-IRON TABLETS/LIQUID

bottles of 100 *bottles of 12 fl. oz.*

Each tablet or teaspoonful of liquid contains ferrous sulfate, 195 mg. (3 gr.), and molybdenum oxide, 3 mg.

DOSAGE: Adults—2 tablets or 2 teaspoonfuls of liquid t.i.d.

Children—1 tablet t.i.d. or ½ to 1 teaspoonful t.i.d.

For protection against iron deficiency during infancy—

MOL-IRON DROPS

well tolerated, highly palatabl

bottles of 15 cc. and 50 cc. with calibrated dropper

Each cc. contains 125 mg. (2 gr.) ferrous sulfate and 2 mg. molybdenum oxide.

DOSAGE: Children up to 6 years—0.3 cc.; over 6 years—0.6 cc. daily.

For iron-deficiency anemias complicated by impaired absorption of iron—

MOL-IRON c̄ VIT. C TABLETS

bottles of 100

Each tablet equals one Mol-Iron tablet plus 75 mg. ascorbic acid.

DOSAGE: As required—1 or 2 tablets t.i.d.

For best results—choose the right iron

White

White Laboratories, Inc., Kenilworth, New Jersey

The Solution to Your Dermatologic Problems!

DISEASES *of the* SKIN

by

RICHARD L. SUTTON, JR.
A.M., M.D., F.R.S.(Edin.)

11th Edition. 1479 pages, 1972 illustrations.
Price, $29.50

Here is assembled in one monumental volume all the technical information necessary for understanding and management of dermatologic conditions. The various skin conditions discussed are emphasized in proportion to their incidence. In each situation you are given the correct diagnosis—then the treatment best suited to the condition is fully explained.

It is comprehensive, yet condensed. The illustrations (1479 of them) are an atlas wherein all ordinary and many extraordinary dermatoses may be identified. The book includes features of a dictionary and an encyclopedia. It is a guide to what may be found in an extensive medical library. It is a systematization written by an inquisitive practicing physician. The order of presentation uses causation as a guide to classification. Concepts of disorders of the skin are tied with general medicine and biology.

All known skin diseases, including the exanthems, are discussed and adequately indexed. Diseases are grouped by cause when this is known, and by morphology when it is not. The outlines of therapy are practical, explicit, and comprehensive.

What distinguishes this text is the level of writing. It is clearly a work of superb scholarship and deserves its reputation of being a classic not only in the field of dermatology but also among medical literature as a whole.

THE C. V. MOSBY COMPANY **Date**----------
3207 Washington Blvd., St. Louis 3, Mo.

Gentlemen: Send me Sutton "DISEASES OF THE SKIN," priced at $29.50. ☐ Attached is my check. ☐ Charge my account.

Dr. ---------- Street ----------

City ---------- Zone ------ State ----------

PED-12-57

Announcing

The Wyeth Laboratories Pediatric Residency Fellowship Program

THE need for increased specialization in the diseases and disorders of the young is widely acknowledged. In response to this need, Wyeth Laboratories has inaugurated a program of residency assistance.

INITIALLY, fellowship grants will be awarded annually to 20 qualified interns or physicians who have recently completed their internships. Each grant will provide $2400 yearly for two years of residency training at a properly accredited hospital of the recipient's choice. The selection of recipients will be based on pediatric inclination, personal character, academic competence, and financial need. Awards will be limited to citizens of the United States or Canada.

NAMES of the first grantees will be announced in the spring of 1958 for fellowships taking effect on the following July 1.

ALL applications for grants will be processed by the Selection Committee, composed of distinguished physicians in active pediatric service. Wyeth Laboratories has no part in the selection of recipients. The Chairman of the Selection Committee, to whom requests for applications or for further information should be addressed, is Philip S. Barba, M.D., School of Medicine, University of Pennsylvania, Philadelphia 4, Pa.

Philadelphia 1, Pa.

"Christmas! Bah! Humbug!"

The man in the wheel chair leaned into the microphone. "Christmas!" he snarled. "Bah! Humbug!" And, as they had in Christmases past, millions of young listeners chilled at the mental picture of the baleful Scrooge.

It was a Christmas institution, back in the Forties, this annual reading of Charles Dickens' classic. Its reader was something of an institution himself. In his turbulent lifetime he had been an unsuccessful painter but a good amateur second-baseman, a composer whose music was played by the New York Philharmonic, and a model for Frederick Remington.

To most people, though, he was Lionel Barrymore, the actor, and they loved him.

He was both crusty and kindly (he loved reading "A Christmas Carol"), adventurous, stubbornly independent in thought and outlook. And game as they come. Although an accident in 1936 imprisoned him in a wheel chair, he went resolutely on—working in motion pictures and making public appearances for nearly twenty years more.

No question but that Lionel Barrymore was one-of-a-kind. Yet the qualities so richly combined in him exist in a large measure among all the 170 million of us who call ourselves Americans.

They're why we are what we are, why our country is one of the strongest on earth. And why there is no wiser investment than an investment in America—through U. S. Savings Bonds, which guarantee the safety of your savings, up to any amount, and the rate of your return. Start buying Bonds today, through Payroll Savings or where you bank. And hold onto them!

Now Savings Bonds are better than ever! Every Series E Bond purchased since February 1, 1957, pays 3-¼% interest when held to maturity. It earns higher interest in the early years than ever before, and matures in only 8 years and 11 months. Hold your *old* E Bonds, too. They earn more as they get older.

PART OF EVERY AMERICAN'S SAVINGS BELONGS IN U.S. SAVINGS BONDS

The U. S. Government does not pay for this advertisement. It is donated by this publication in cooperation with the Advertising Council and the Magazine Publishers of America.

INDEX TO ADVERTISERS

Please mention "The Journal of Pediatrics" when writing to our advertisers—It identifies you

Abbott Laboratories (Vi-Daylin) ..... 2 & 3
Abbott Laboratories (Compocillin-V) ..... 28 & 29
Air-Shields, Inc. (Croupette) 14
American Bakers Association (Enriched Bread) 66
American Meat Institute 32
American Sterilizer (New Penn "600") 22
Ames Company, Inc. (Diatussin) 4
Arnar-Stone Laboratories, Inc. (Sillcote) 84
Articles to Appear 90
Aveeno Corporation (Colloidal Oatmeal & Ointment) ..... Insert between pages 48 & 49
Ayerst Laboratories (Cytoferin) 8

Baker Laboratories, Inc., The (Varamel) 54
Ball Brothers Company (Hygeia Nurser) 85
Baxter Laboratories, Inc. (Controlled Volume Unit) 60
Borcherdt Company (Malt Soup Extract) 83
Borden Company, The (Bremil) ..... Fourth Cover
Bristol Laboratories, Inc. (Tetrex) ..... 36 & 37
Bristol Laboratories, Inc. (Tetrex) ..... Insert between pages 64 & 65
Bristol Laboratories, Inc. (Azotrex) ..... 80 & 81
Bristol-Myers Company (Ammens Powder) 38
Brown Shoe Company (Propr-bilt) 40
Burroughs Wellcome & Company (USA) Inc. (Antepar) 68

Carnation Company & Subsidiaries (Evaporated Milk) 91
Carpenter Shoe Company, Inc., The (Self-Starters) .. 95
Central Drug (Diaper Pure) 96
Chesbrough, Inc., G. W. (Pre-Walker) 96
Chicago Pharmacal Company (Katrasul) 20
Ciba Pharmaceutical Products, Inc. (Serpasil Elixir) .. 1
Corn Products Refining Company (Karo Syrup) 12

Desitin Chemical Company (Desitin Ointment) 18
Dome Chemicals, Inc. (Acid Mantle) 50
Durst & Company, Inc., S. F. (Pedameth) 13

Eaton Laboratories (Furadantin) ..... 26 & 27
Electric Steam Radiator Corporation, Subsidiary of Landers, Frary & Clark (Electresteem All-Nite Vaporizer) 82

Fuller Pharmaceutical Company (Tucks) 89

Herbst Shoe Manufacturing Company (Child Life Shoes) ..... 30 & 31

Jackson-Mitchell Pharmaceuticals, Inc. (Hi-Pro) 43
Jackson-Mitchell Pharmaceuticals, Inc. (Goat Milk) .. 45
Johnson & Johnson (Baby Lotion) Insert between pages 8 & 9
Johnson & Johnson (Baby Lotion) 9
Johnson & Johnson (Liquiprin) 25
Johnson & Johnson (Baby Powder) 33

Kannengiesser & Company (Kanana Banana Flakes) .. 11
Kinney & Company, Inc. (Emetrol) 75

Lederle Laboratories (Achromycin) 65
Leeming & Company, Inc., Thos. (Piperazate Wafers) 48
Leeming & Company, Inc., Thos. (Nephenalin) 93
Lilly and Company, Eli (V-Cillin Drops) 16
Lilly and Company, Eli (Ilotycin-Sulfa) 47
Lilly and Company, Eli (V-Cillin Pediatric) 78
Lloyd Brothers, Inc. (Doxinate) 58

McNeil Laboratories, Inc. (Tylenol) 59
Maltbie Laboratories, Division Wallace & Tiernan, Inc. (Caldesene) 64
Mead Johnson & Company (Vi-Sol Vitamin Family) .. 35
Mead Johnson & Company (Deca-Mulcin & Deca-Vi-Caps) 41
Mead Johnson & Company (Deca-Vitamin Family) .. 63
Mead Johnson & Company (Tempra) 76
Merck Sharp & Dohme (Remanden) 69
Merck Sharp & Dohme (Redisol) 94

Parke, Davis & Company (Paladac) 5
Pet Milk Company (Evaporated Milk) 79
Pfizer Laboratories (Tyzine) 49
Pitman-Moore Company (Arobon & Intromycin) .. 6 & 7
Pitman-Moore Company (Neo-Polycin) ..... Insert between pages 16 & 17
Pitman-Moore Company (Novahistine Elixir) 19
Procter & Gamble Company (Ivory Snow) 67

Reed & Carnrick (Tarcortin) 44
Rhinopto Company (Rhinall Cough Syrup) 89
Riker Laboratories (Medihaler-Epi & Medihaler-Iso) 21
Roche Laboratories (Vi-Penta) ..... Second Cover
Roche Laboratories (Lipo Gantrisin) ..... Insert between pages 32 & 33
Roerig & Company, J. B. (Atarax) 55
Ross Laboratories (Similac) 34

Smith, Kline & French Laboratories (Trophite) 15
Smith, Kline & French Laboratories (Compazine) .. 104
Squibb & Sons, E. R. (Theragran) 46
Strasenburgh Company, R. J. (Tussionex) 23
Swift & Company (Fruit-Flavored Meats) 24

United States Savings Bonds 102
Upjohn Company, The (Zymabasic drops) 61

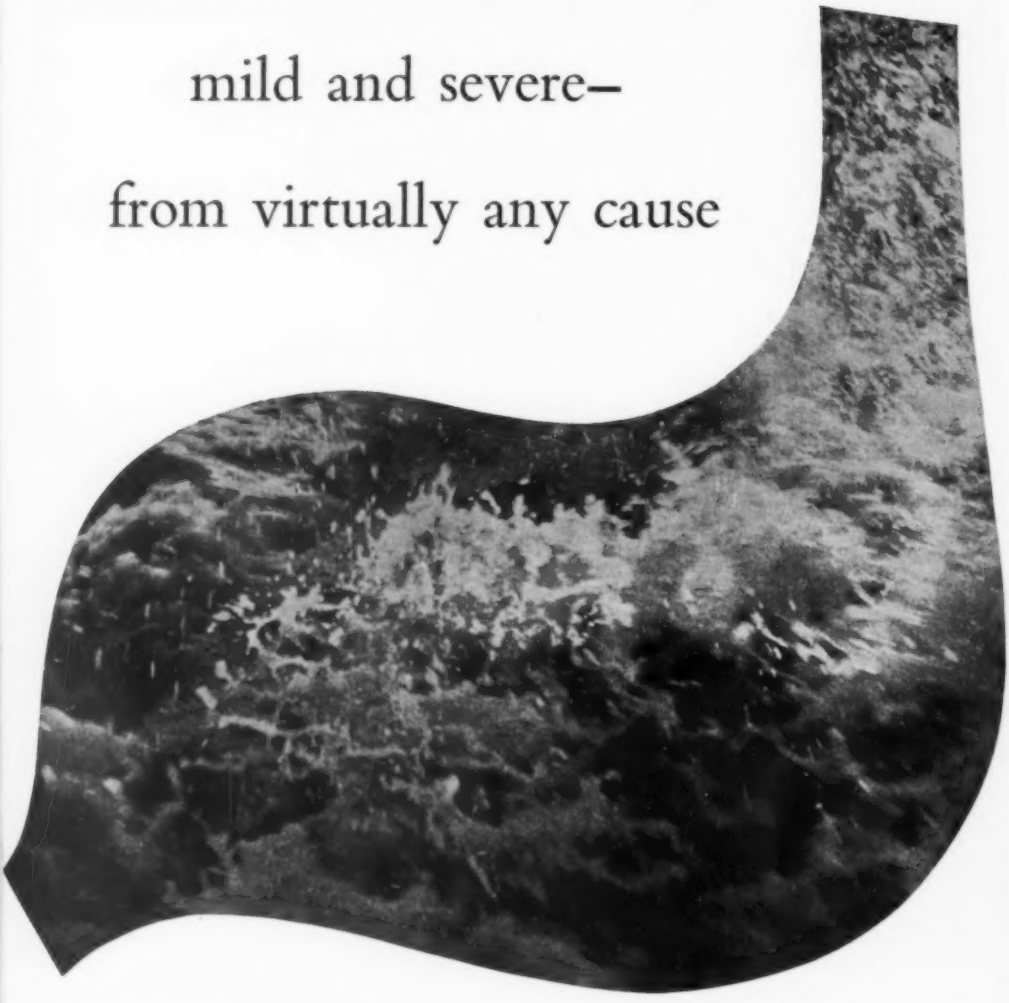
Walker Laboratories, Inc. (ADCETS) 74
Wander Company, The (Ovaltine) 52
Warren-Teed Products Company, The (Tympagesic Ear Drops) 17
Webster Company, The William A. (Gentian-EV) .. 10
Webster Company, The William A. (Aquachloral) 77
Westwood Pharmaceuticals (Fostex) 62
Westwood Pharmaceuticals (Lowila Cake) 82
White Laboratories, Inc. (Cod Liver Oil Concentrate Tablets) 56
White Laboratories, Inc. (Vitamin A and D Ointment) 84
White Laboratories (Otomide & Otodyne) 94, 95
White Laboratories (Mol-Iron) 80, 81
Winthrop Laboratories (Alevaire) 51
Wyeth Laboratories (Sulfose) 39
Wyeth Laboratories (Phenergan) 42
Wyeth Laboratories (Pen-Vee-Sulfas) 53
Wyeth Laboratories (Pen-Vee-Oral) 57
Wyeth Laboratories (S-M-A) 70, 71, 72, 73
Wyeth Laboratories (Polymagma) 87
Wyeth Laboratories (Announcement) 101

While every precaution is taken to insure accuracy, we cannot guarantee against the possibility of an occasional change or omission in the preparation of this index.

stops nausea and vomiting–

mild and severe–

from virtually any cause



*Compazine**

tablets, ampuls, Spansule† capsules

Smith, Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off. for prochlorperazine, S.K.F.
†T.M. Reg. U.S. Pat. Off. for sustained release capsules, S.K.F.

CONTENTS FOR DECEMBER, 1957

The Roentgenographic Findings Associated With Neuroblastoma. Charlotte F. Hansman, M.D., and Bertram R. Girdany, M.D., Pittsburgh, Pa. ---- 621

Urinary Excretion of Fluoride by Children Aged Two Through Five Years Using a Stannous Fluoride-Containing Dentifrice in a Natural Fluoride Area and a Nonfluoride Area. Richard A. Schweinsberger, M.S., and Joseph C. Muhler, D.D.S., Ph.D., Bloomington, Ind. ---- 634

Interstitial Plasma Cell Pneumonia and Pneumocystis Carinii. Aníbal Ariztía, M.D., Werner Bustamante, M.D., Luis Moreno, M.D., Armando Doberti, MD., Clara Román, Tulio Pizzi, M.D., and María Díaz, M.D., Santiago, Chile ---- 639

Comparison of Ocular Reactions Using Penicillin and Bacitracin Ointments in Ophthalmia Neonatorum Prophylaxis. A. M. Margileth, Commander (MC) USN, Chelsea, Mass. ---- 646

Formation of Mucous Membrane Lesions Secondary to Prolonged Use of One Per Cent Aqueous Gentian Violet. Eugene L. Slotkowski, M.D., Chicago, Ill. ---- 652

Novobiocin in Common Pediatric Infections. Angella D. Ferguson, M.D., Gertrude C. Teixeira, M.D., and Roland B. Scott, M.D., Washington, D. C. ---- 655

Apparent Sensitization to Novobiocin. James G. Hughes, M.D., Memphis, Tenn. ---- 664

The Roentgenographic Diagnosis of Geophagia (Dirt-Eating) in Children. Joseph E. Gardner, M.D., and Fethi Tevetoğlu, M.D., Corpus Christi, Texas ---- 667

Ear Studies in the Newborn Infant. M. S. McLellan, M.D., and C. H. Webb, M.D., Shreveport, La. ---- 672

Growth and Development. I. Relation of Birth Weight in Negro Infants to Sex, Maternal Age, Parity, Prenatal Care, and Socioeconomic Status. E. Perry Crump, M.D., Carrell P. Horton, M.A., Jitsuichi Masuoka, Ph.D., and Donnalda Ryan, B.S., Nashville, Tenn. ---- 678

Surgical Treatment of Pyloric Stenosis in an Infant With Hemophilia A. J. I. de Bruijne, M.D., S. van Creveld, M D., and R. Steendijk, M.D., Amsterdam, The Netherlands. With the Technical Assistance of Miss P. E. Groen ---- 698

Sporadic Cretinism With Goiter Occurring in Identical Twins. Henry F. Frierson, M.D., John C. Hawk, Jr., M.D., and Margaret Q. Jenkins, M.D., Charleston, S. C. ---- 704

Infant and Child Mortality in a Korean Rural Area. Duk Jin Yun, M.D., M.P.H., Seoul, Korea ---- 709

Clinical Pathological Conference

The Children's Medical Center, Boston, Mass. ---- 716

Medical Progress

Hyaline Membrane Disease. Paul Curtis, M.D., New York, N. Y. ---- 726

Comments on Current Literature

Natural Immunity to Poliomyelitis. Russell J. Blattner, M.D., Houston, Texas ---- 742

Correspondence

Correspondence ---- 745

News and Notes

News and Notes ---- 748

Books

Books ---- 749

Editor's Column

A Journal of Pediatrics Fund for Furthering Pediatrics ---- 751

Is Pediatric Practice a Satisfying Lifework? ---- 751

Index

Index ---- 755

(Editorial and Business Communications on page 88)

natural tranquility*

characteristic of babies fed

Borden's Bremil®

nutritionally complete... physiologic
...a clinical counterpart of breast milk
...reasonable cost

avoids excoriated buttocks
• minimizes digestive upsets
• virtually eliminates hyperirritability
due to subclinical tetany
• avoids excessive renal solute load,
thus lessening the dangers of dehydration
should periods of stress occur
standard dilution from birth—
1 level measure to 2 fl.oz. hot water

BREMIL • MULL-SOY • DRYCO • BETA LACTOSE • KLIM
products of
BORDEN'S PRESCRIPTION PRODUCTS DIVISION,
350 MADISON AVENUE, NEW YORK 17

*parents of babies fed BREMIL are naturally tranquil, too

7709